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THE NEW NUCLEAR PHYSICS AND MEDICINE

CALDWELL LECTURE, 1941*

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INTRODUCTORY REMARKS

By EUGENE P. PENDERGRASS

Once again we are assembled to hear the presentation of our annual Caldwell Lecture. This Lecture, founded in 1940 in memory of Eugene Wilson Caldwell, a distinguished pioneer and American radiologist, is delivered each year by one whom the Society wishes to honor and who has contributed to the progress of radiology.

The story of the rapid development of radiology, made possible by the practical applications of recent discoveries in modern physics, is of itself nothing short of an absorbing romance. Physical science, through the startling discoveries of the x-rays by Roentgen, the recognition of radioactivity by Becquerel, the discovery of radium by the Curies, the enunciation of the theory of relativity by Einstein, the artificial production of radioactivity by Joliot and Curie, the discovery of heavy hydrogen by Urey *et al.*, and the development of the cyclotron by Dr. E. O. Lawrence and his associates, are constantly providing medicine, and radiology in particular, with new tools to attack the problems of human suffering. Indeed, the dreams of the ancient alchemists, who sought to turn base metal into gold, have been surpassed; for the modern physicist, with the cyclotron, is now making something vastly more precious and useful—the artificial radioactive substances.

Tonight, it is particularly fitting, that the Caldwell Lecture is to be delivered by one who with his distinguished brother, Dr. E. O. Lawrence and their associates, is providing medicine, biology and physics with agents that should revolutionize our knowledge of the structure of the world and everything that lives in it.

Dr. Lawrence, in planning his education, so arranged it that he has been exposed to teachers in widely separated institutions. He received his A.B. degree from the University of South Dakota; his medical degree from Harvard; he was a student interne in the Robert Breck Brigham Hospital, Boston; surgical interne, Peter Bent Brigham Hospital; assistant resident in medicine, Strong Memorial Hospital, Rochester, N. Y. and instructor in medicine, Yale University Medical School. As Director of Medical Research at the Crocker Radiation Laboratory, Berkeley, California, Dr. Lawrence has been interested in the experimental production of tumors and leukemias in animals, clinical investigations in the field of neoplastic disease, and has carried out a number of studies concerning the action of radioactive materials in animals and man. I have the honor and pleasant duty of presenting to you our Caldwell Lecturer of the evening, Dr. John H. Lawrence, of the University of California.

* The Twenty-second Caldwell Lecture, delivered at the Forty-second Annual Meeting of the American Roentgen Ray Society, Cincinnati, Ohio, September 23–26, 1941.

CALDWELL LECTURE

I WISH to thank the members of the American Roentgen Ray Society for the privilege of giving the Caldwell Lecture, and to make it clear that I accept this honor not as an individual but as a representative of a group of physicists, biologists, and medical men, all of whom are intensely interested in the applications of physics to medical and biological problems.

As you all know, the intense study of the atom and of the atomic nucleus carried out during the past few years by physicists throughout the world has resulted in contributions of great value to biology and medicine. Among the most important of these is the induction of artificial radioactivity in all the chemical elements which in the form of labeled or tagged isotopes are being applied in biology as well as investigative and therapeutic medicine. During their as yet young life (the tagged isotopes were produced for the first time in 1934), enough work has already been done by various investigators to indicate that they will rival the microscope in scientific usefulness. In addition, the physicists have given us a new form of penetrating radiation similar in some respects to high voltage roentgen rays, namely, the neutron ray.

This evening I should like to say a few words regarding the development of artificial radioactivity and of neutron rays; then I shall pass on to a discussion of the nature of these new elements with a demonstration of several of them and of the methods of their production, and finally I shall speak in more detail of their applications in biological and medical investigation and therapy. These applications are already so extensive that it is impossible to cover the field completely. However, I shall attempt to summarize some of the more important work after describing and giving examples of the various techniques which have been developed. In conclusion, I shall discuss several of the new elements which localize or concentrate in certain tissues, I shall make a few remarks on their use in the treatment of disease, and finally I shall discuss briefly the biological and therapeutic effects of neutron rays.

The effectiveness of radium and roentgen rays in therapy is due to the ionization produced in the tissue undergoing irradiation. The rays from radium and roentgen radiation have the properties of penetrating tissue to a greater or lesser degree and of producing ionization within the tissues. Because of the relatively great sensitivity of some neoplastic tissues to the biological changes thus produced, roentgen rays and the radioactive substances have become extremely valuable in the treatment of neoplastic disease—*the basis for the specialty of radiation therapy*. In addition, the radiations emitted from radioactive elements, such as radium, permit detection of these elements by physical instruments such as the electroscope and the Geiger counter. Every radiologist at some time in his life uses a Geiger counter or an electroscope to aid in finding radium which has been lost. The presence of radium within the tissues of experimental animals may be detected by similar methods. At autopsy the exact proportion of radium present in various tissues can be determined physically either by counting the radiations emitted with the use of a Geiger counter, which we shall demonstrate later, or by measuring the ionization produced by the radiation with an electroscope. As you all know, Dr. Harrison Martland, of Newark, has carefully studied the unfortunate cases of radium poisoning both in life and after death by this method. Knowledge of these facts and of the fact that one of the decomposition products of radium, that is radium D, is an isotope of lead, enabled Hevesy, the physicist from Copenhagen, to study the distribution of lead in plants. Although his work suggested a powerful method of investigation to the biologist, it unfortunately was limited to following the metabolism of the naturally occurring radioactive substances which are few and relatively unimportant in biological

systems. If the biologist, aware of the possibilities of radioactivity, could be given by the touch of a magic wand anything he desired, he might say: "Make all the naturally occurring elements radioactive. Give me radio-phosphorus and radio-sulfur, to unravel the secrets of cell metabolism since these radioactive atoms, tagged by their emitted radiations may be traced wherever they go, and their speed may be determined. Give me radio-iron and radio-sodium, so that I may delve deeper into the problems of blood formation and anemia and into those of the utilization of sodium chloride which is so important in acid-base and water metabolism. Make the duration of the radioactivity in these elements suitably short, so that they may be given in small quantities as tracers to animals and to man without danger. Make all the elements radioactive in large quantities, so that they may be used like radium in therapy."

Strange as it may seem, almost all of these desires already have been fulfilled. In 1934, Joliot and Curie,[20] son-in-law and daughter of Pierre and Marie Curie, reported that they had produced artificially in the laboratory, radio-nitrogen, radio-silicon, and radio-magnesium. The development of the cyclotron by my brother, Ernest Lawrence, and his associates, make it possible to produce artificially radioactivity in all the chemical elements in large quantities adequate for both "tracer" and therapeutic investigations.[23]

Before discussing the biological applications, I shall point out certain more or less obvious characteristics of the new radioisotopes. Here in my hand are weak samples of three different artificially induced radioactive substances. This one is yttrium, this one iodine, and this one, phosphorus. When they are held up to the Geiger counter you can hear that all three give off rays. The gamma rays from yttrium pass directly through large thicknesses of material, for they are so penetrating that neither a book nor my hand can stop them. Similarly, iodine gives off gamma rays which penetrate deeply, but it also emits less penetrating rays, i.e., beta rays, which can be cut out by my hand. Phosphorus, on the other hand, gives off only beta rays which are easily absorbed. Similarly, all the other artificially induced radio-elements emit rays like the rays from radium. But here their resemblance to radium ceases. Each one of these new radio-elements remains chemically the same as its inactive relative. Chemically radio-iodine is like ordinary iodine, radio-iron is like ordinary iron and cannot be distinguished from it and so it is with all the elements. Thus, the rays emitted tag or label these elements so that the investigator is able to study the absorption, distribution, excretion, and secretion of all the chemical elements in plants and animals in normal and disease processes. For the first time, he is able to differentiate in the plant or animal the portion of a given element which was injected or administered in the diet or in some compound, from that which was already present. Because of the radiations it emits, he is able to follow its course through the plant or animal. When one considers the number of elements important in life processes, the great value of the artificially radioactive isotopes to biology is apparent. Finally, I wish to emphasize that tracer doses or quantities of these isotopes, in contrast to therapeutic doses, are extremely small and harmless and produce no physiological changes in the organism. In all tracer investigations it is important that very weak activities be used.

In Figure 1 is seen a typical reaction which takes place when an element is bombarded with deuterons, the bullets usually employed in the cyclotron. It depicts a deuteron striking ordinary sodium which has an atomic weight of 23. The neutron half of the deuteron is captured making sodium 24 which is radioactive but retains the chemical properties of ordinary sodium. When radioactive elements are used in biological investigations, they can be converted beforehand into various

compounds. For instance, in the case of radio-phosphorus, disodium phosphate is usually the compound made; on the other hand, radio-sodium is usually converted into sodium chloride. Likewise, these elements may be built into more complicated compounds before they are used. For instance, radio-sulfur has been used in synthesizing vitamin B for tracer studies.

In the application of these isotopes to biological and medical problems, three

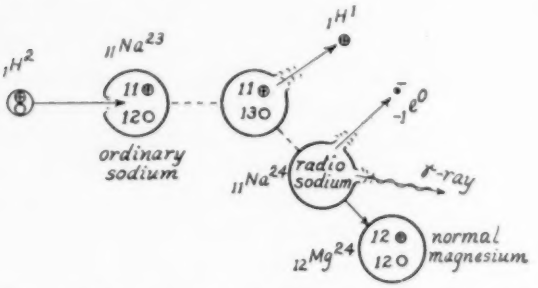

FIG. 1. The reaction taking place when sodium is made radioactive by bombardment with deuterons accelerated in the cyclotron. Sodium 23 takes on a neutron, converting it into sodium 24, which, however, has the same charge on its nucleus as sodium 23, and consequently maintains the chemical properties of sodium. Sodium 24 is radioactive and on the emission of a beta ray becomes normal magnesium. This reaction is typical of many which take place when elements are made radioactive.

general techniques have been developed. The first, which is the most widely used and which is applicable to all of the radio-elements, consists in the administration of a compound of a given element to a plant or animal and in the determination of its distribution in various tissues or materials at different periods of time. In order to determine the percentage of uptake of the element, the plant or animal is sacrificed and the radiations coming from any individual tissue are counted. The contributions of Whipple and his associates,[10,11,12,13,25] and of Austoni and Greenberg[2] in the use of radioactive iron serve as examples of this technique. These workers have shown the fallacy of the hypothesis that the amount of iron retained in the body is regulated by varying rates of excretion. When radioactive ferric salts were given orally to normal and anemic animals and the animals were sacrificed at various periods thereafter, the uptake of the tagged iron, as determined by Geiger counter measurements, was from 4.1 to 12.7 per cent in the anemic animals and from 0.08 to 0.24 per cent (very much less) in the normal controls. These studies indicate that the uptake of the administered radio-iron is determined by the need of the body for iron, and that in the anemic (iron deficient) animals, the total absorption of the labeled iron as well as the relative proportion of the absorbed radio-iron in the blood is much greater than in the control animals. In later experiments, these investigators studied the metabolism of tagged iron following its intravenous administration in normal and anemic dogs. They observed that the rates of elimination of the radio-iron were very slow in both groups and that no significant differences existed in the rates of excretion in normal and anemic dogs. They concluded that the body controls the level of its iron stores by regulating the quantity of the iron absorbed from the digestive tract rather than by its capacity to eliminate the assimilated iron. It was also shown that the absorbed radio-iron in the blood was converted almost entirely into the iron-containing protein, hemoglobin, and that the percentage of uptake is much greater when small amounts of iron are administered. All these investigations contribute to a better understanding of iron metabolism and to improvements in the treatment of the anemias.

The value of the first technique is again demonstrated by the extensive work of Ruben, Hassid, Kamen, and associates,[3,27,28] who used radio-carbon in the study of photosynthesis, and related processes, by growing various plants and bacteria in an atmosphere of radioactive carbon dioxide both in the dark and in the light, by extracting for simple and complex compounds of carbon, and by measuring these compounds for the activity of the carbon built into them. For instance, they demonstrated that plants and algae containing chloro-

phyll have the ability to assimilate a small but measurable proportion of tagged carbon dioxide from the air in the complete absence of light. The carbon dioxide was reduced to a carboxylic acid which was attached to a large complex molecule. They also observed that nonphotosynthetic organisms (cells which do not contain chlorophyll and do not utilize light in their metabolic processes) have the capacity to reduce carbon dioxide. For example, in bacteria grown in a medium containing carbon dioxide, they have observed the production of proprionic and acetic acids containing labeled or radioactive carbon. The evidence so far obtained by these investigators has led to the suggestion that all living organisms have the capacity to reduce carbon dioxide.

Erf[5] and Erf and Pecher[9] have carried out some interesting studies with the radioactive isotopes of calcium, strontium, and iron in cows. Tracer amounts of strontium are handled in the body in the same manner as calcium. These workers have shown that when compounds of calcium, strontium, or iron are administered to cows, these substances appear rather rapidly in the milk during the next twenty-four hours. These results emphasize the relationship of the diet of the cow to the mineral content of milk which is such an important food, particularly for infants.

Finally, the first technique, i.e., the radio assay of biological materials such as plants and tissues, is perhaps best demonstrated by the extensive investigations carried out with radioactive phosphorus. This element can be made easily and in large quantities by the cyclotron and has a suitably long half-life, i.e., 14.3 days. It was first used by Chiewitz and Hevesy[4] in studies of the phosphorus metabolism of rats. During the past few years it has been used by many workers in different fields. We shall speak later of its application to medical therapy. There is not sufficient time even to begin to review the work done with this isotope, but perhaps it is of interest to mention some studies on the *metabolism of tumor tissue* in animals.[21,24,32] Table 1 shows that the total content of chemical phosphorus in the tissues of mice is the same whether these tissues contain tumor cells or not. In other words, one cannot differentiate the two kinds of tissue by straight chemical analysis. In Figure 2 it is shown, however, that when radioactive phosphorus is used to label the phosphorus content, the metabolism of normal tissue differs considerably from that of tumor tissue. It is to be noted that leukemic infiltration is always associated with a high uptake of labelled phosphorus chiefly in the nucleoprotein fraction. Similarly, Figure 3 shows that the uptake by three different tumors in mice, as compared with the uptake of normal tissues, is high. In general, it has been found in animals that wherever there are tumors, the phosphorus turnover is high. This is due to the fact that the phosphorus atoms are synthesized into new organic compounds such as nucleoproteins and phospholipids. These findings have led to the use of radio-phosphorus in the treatment of disease.

The second method for the application

TABLE I

TISSUE	NO. OF ANIMALS	MEAN MG P/G
LIVER N	46	3.86
LIVER L	39	3.59
SPLEEN N	22	4.58
SPLEEN L	39	4.77
LYMPH N	40	5.67
LYMPH L	27	5.81
BONE N	40	75.6
BONE L	28	73.2
MUSCLE N	37	3.02
MUSCLE L	53	3.00
TUMORS	29	4.14

These figures show the comparative phosphorus content of normal (N) and leukemic (L) tissues. It is noted that leukemic infiltration does not influence significantly these values.

of radio-isotopes to biology is autoradiography. After the administration of the isotopes, sections of the biological materials are placed for varying periods of time against photographic films. The clouding of the film by the beta rays from the deposited atoms gives a photograph of the distribution of the atoms in the biological material studied. For instance, in Figure 4 is seen the distribution of phosphorus atoms in the leaves of a tomato plant grown in a solution containing small quantities of sodium radioactive phosphate. This technique, the plant physiologists say, is proving very helpful in their studies of the absorption and movement of various essential elements in plants.

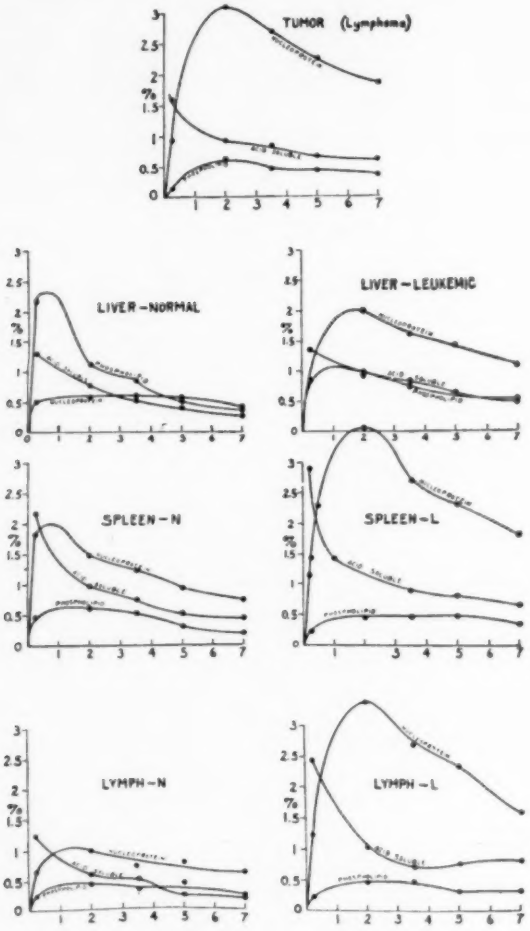

FIG. 2. The comparative uptake of phosphorus, as percentage of injected dose, in various normal and leukemic tissues of mice. Leukemic infiltration is always associated with a high uptake, particularly in the nucleoprotein fraction.

The third method used is the *in vivo* technique developed largely by Dr. J. G. Hamilton. It consists of the study of the absorption, distribution, and deposition of various chemical elements in the intact animal or human being and has the obvious advantage of making the sacrifice of the experimental subject unnecessary, a procedure which is, of course, not advisedly employed in the case of human beings. The subject receives orally or parenterally a tracer dose of a given element, and thereafter the absorption and distribution of the element can be followed by placing the Geiger counter over the part of the body to be studied. An example of the value of this technique is the surprising finding that some elements appear in the fingers within a few minutes after oral administration,[15] indicating very rapid absorption and transportation.

The three techniques described have been used with many elements. Those employed so far in biological or medical investigations are listed in Table II. The first is *radioactive hydrogen*, *hydrogen 3*, which is

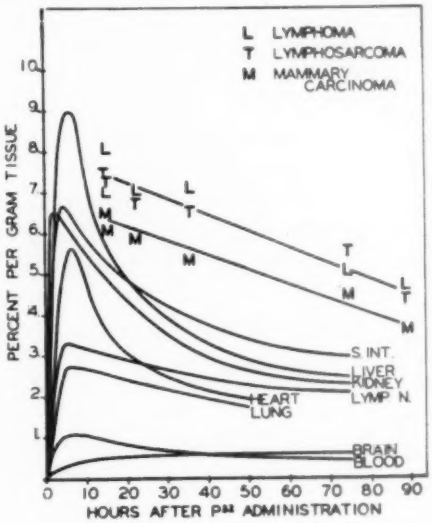

FIG. 3. The percentage of injected radioactive phosphorus (as Na_2HPO_4) in neoplastic tissues as compared with normal tissues of mice. Each animal carried three subcutaneously implanted tumors.

even heavier than *heavy hydrogen*. It emits beta rays and has a half-life of thirty years. This radioactive element is now being synthesized into dyes. After the dyes have been administered, the distribution in various tissues is studied. It is also proving valuable in chemical research for tagging various reactions. *Carbon 11*, having a half-life of twenty-one minutes, is the element used by Kamen and his associates in studies of photosynthesis. *Carbon 14* with a half-life of over a thousand years may prove very valuable when production difficulties have been overcome. *Nitrogen 13*, with an extremely short half-life, 9.93 minutes, has been used in the study of nitrogen fixation in nonleguminous plants. *Sodium 22* and *24* have half-lives of three years and 14.8 hours respectively and are used extensively in tracer work. Similarly *magnesium 27*, although it has a very short half-life, is valuable in tracer studies. Phosphorus, with a half-life of 14.3 days, has been widely used, as pointed out previously. Next we note *sulfur 35* which emits beta rays and has a half-life of eighty-eight days.

Fig. 4. Autoradiograph of tomato plant grown in solution containing sodium radio-phosphate. (Courtesy of Dr. Perry Stout.)

Table II

List of Radioactive Elements Which Are Being Used in Biological and Medical Investigations

Radio Active Element	Type of Radiation	Half-Life
$_{1}H^{3}$	B^-	30.0 yr.
$_{6}C^{11}$	B^+	21.0 min.
$_{6}C^{14}$	B^-	1000.0 yr.
$_{7}N^{13}$	B^+, γ	9.93 min.
$_{11}Na^{22}$	B^+	3.0 yr.
$_{11}Na^{24}$	B^-, γ	14.8 hr.
$_{12}Mg^{27}$	B^-, γ	10.2 min.
$_{15}P^{32}$	B^-	14.3 days
$_{16}S^{35}$	B^-	88.0 days
$_{17}Cl^{38}$	B^-, γ	37.0 min.
$_{19}K^{42}$	B^-, γ	12.4 hr.
$_{20}Ca^{45}$	B^-, γ	180.0 days
$_{25}Mn^{54}$	K, γ	310.0 days
$_{26}Fe^{59}$	B^-, γ	47.0 days
$_{27}Co^{55}$	K, γ, e^-, B^+	270.0 days
$_{29}Cu^{64}$	B^-, B^+, K	12.8 hr.
$_{30}Zn^{65}$	B^+, K, γ, e^-	250.0 days
$_{33}As^{76}$	B^-, B^+, K, γ	26.8 hr.
$_{33}As^{74}$	B^-, B^+, γ	16.0 days
$_{35}Br^{82}$	B^-, γ	34.0 hr.
$_{37}Rb^{86,88}$	B^-	18.0 days
$_{38}Sr^{89}$	B^-	55.0 days
$_{53}I^{131}$	B^-, γ	8.0 days
$_{85}{}^{211}$	K, α	7.5 hr.

It has been used by Tarver and Schmidt[30] in studies of amino-acid synthesis and by others as mentioned previously. Going down the list, *chlorine*, *potassium*, *manganese*, *calcium*, *iron*, *cobalt*, and *copper*—all are being used in biological studies by the various techniques described. Also listed are *zinc*, *arsenic*, *bromine*, *rubidium*, and then *strontium* and *iodine*, which will be discussed in more detail later, and finally the newly discovered *element 85* which is particularly interesting since physiologically it acts like iodine.[16]

Several of the radioactive elements are especially noteworthy because they tend

to localize selectively in certain tissues. These are: *radioactive iron* which localizes in the red blood cells and in the bone marrow; *radioactive phosphorus* which localizes in the bone and bone marrow and also to a relatively high degree in spleen, lymph nodes, and liver; *radio-iodine* which concentrates in the thyroid, and *radioactive strontium* and *calcium*, both of which localize more or less exclusively in the bone. It is also interesting to note that strontium

TABLE III

UPTAKE AND RETENTION OF A CHROMIC PHOSPHATE SUSPENSION

INTRAVENOUS ADMINISTRATION

4 days after $CrPO_4$ Administration

Dog (8.5 Kilogram)		Mouse (22 Gram)	
% per whole organ:		% per whole organ:	
liver	80.0	liver	89.0
spleen	8.3	spleen	8.0
lung	1.8	lung	2.9
% per 100 gm. of tissue:		% per gram of tissue:	
liver	25.6	liver	83.0
spleen	24.5	lung	37.0
lymph nodes	0.45	spleen	32.0
lung	0.41	femur	3.3
bone marrow	0.35	lymph nodes	1.1
pituitary	0.26	thymus	1.1
muscle	< 0.1	muscle	< 0.1
kidney	< 0.1	kidney	< 0.1

MOUSE --- % $CrPO_4$ PER WHOLE ORGAN

	3 days	5 days	30 days
liver	89.0	87.0	81.0
spleen	8.0	7.2	4.3
lung	2.9	2.2	3.6

which is in the periodic group with calcium has similar physiological characteristics. Furthermore, recently Jones and Wrobell[22] synthesized a localizing compound, chromic phosphate, with radio-phosphorus. After intravenous injection into mice, they demonstrated its selective uptake by the liver and spleen. This inert colloidal material is taken up by the cells of the reticuloendothelial system and particularly by the Kupffer cells of the liver. Table III, listing the uptake in the various tissues of a dog and a mouse, shows its marked concentration in the liver and spleen.

Hamilton and Soley, *et al.*[14,17,18,19] have been using radioactive iodine in the study of the metabolism of iodine in patients with various types of thyroid disease and in normal subjects by radio-autography and by the *in vivo* technique. In the latter technique, the Geiger counter is held over the thyroid gland after the administration of a compound of the element. They found that the thyroid gland is able to concentrate radioactive iodine to an incredible degree; in some instances there was 5,000 times as much iodine in the thyroid gland as in any other tissue. Dr. Carleton Peirce has agreed to act as a guinea pig, and two days ago took a cocktail of radioactive sodium iodide. I hope that we shall be able to demonstrate that he can concentrate this iodine in his thyroid gland. I shall hold the Geiger counter against the thyroid gland and compare the uptake in the thyroid with the uptake in other parts of the body. You can probably hear that there is a marked selective absorption of iodine atoms in the gland. With very small tracer doses, Hamilton and Soley have been able to classify the different types of thyroid disease according to the uptake of iodine. They demonstrated characteristic curves in normal subjects, in patients with toxic goiters, those with nontoxic goiters, in patients with hypothyroidism without goiter, and those with nontoxic goiter with hypothyroidism. They have made sections of the thyroid glands from patients who had before operation received radioactive iodine and have made autoradiographs of the distribution of the iodine atoms. At the same time, they mounted the same histologically stained sections beside these films so that the histological structure of the gland could be correlated with the deposition of the iodine atoms. It was found that normal thyroid tissue takes up considerable amounts of radioactive iodine, and it seemed to be equally distributed between the cells and the colloid in the central part of the gland, whereas in the case of toxic goiter, the uptake was increased particularly in the region of the colloid. However, they have been disappointed to find that cancer cells lose their ability to take up or concentrate iodine. Therefore the possibility of treating thyroid cancer with radio-iodine is remote. Another interesting feature is the inability of the parathyroid to take up or concentrate iodine. Figure 5 shows sections of the

Fig. 5. Stained section (*right*) and autoradiograph (*left*) of same section of rabbit thyroid and parathyroid. The animal was given radio-iodine orally in the form of sodium iodide previous to being sacrificed. The parathyroid has not accumulated iodine, as indicated by the lack of clouding of the film on the left.

thyroid and parathyroid tissues of a rabbit (right) and on the left the autoradiographs of these same tissues—the animal previously having received radioactive iodine in the form of sodium iodide orally. With larger doses of radioactive iodine, these investigators have been able to destroy selectively the glands in dogs and rabbits. Nevertheless, the other tissues of this animal, including the parathyroids, have not been affected and are normal because the iodine atoms are localized only in the thyroid tissue. This is a bloodless removal of an organ without the aid of the surgeon's knife and without damage to other tissues. These findings suggest the possibility of treating tumors or hyperplasia of the thyroid gland with large doses of radioactive iodine. Indeed, therapeutic attempts are now being made by these investigators on patients with toxic goiter, with extremely satisfactory results to date.

Radioactive calcium, *radioactive strontium*, and *radioactive phosphorus* have very striking localizing properties. The late Dr. Charles Pecher of our laboratory carried out the important pioneer studies with strontium.[26] In the first studies he found that calcium immediately became concentrated in bone with practically no soft tissue deposition. Because of the difficulty of making adequate quantities of radio-calcium, Pecher searched the periodic table and found that strontium was in the same group with calcium. Knowing that radio-strontium could be made in large quantities in the cyclotron, he hoped that physiologically it would behave like calcium, and indeed this is what he found. In Table IV is seen the distribution of these three elements in the bone, muscle, skin, hair, digestive tract, liver, and other viscera of mice which were sacrificed twenty-four hours after administration. In the case of each of the three elements, the greatest concentration is in the bone, but in the case of the first two, *calcium* and *strontium*, the deposition is chiefly skeletal with practically no deposition in the other tissues, whereas the uptake of phosphorus in soft tissues such as muscle, liver and other viscera is considerable. The autoradiograph technique perhaps tends to bring out these points more clearly. Figure 6

Table IV

DISTRIBUTION IN THE TISSUES OF RADIOACTIVE CALCIUM, STRONTIUM AND PHOSPHORUS 24 HOURS AFTER AN INTRAVENOUS INJECTION OF RADIO-CALCIUM LACTATE, RADIO-STRONTIUM LACTATE OR SODIUM RADIO-PHOSPHATE

	Percentage of Dose per Gram Wet Weight					
	Bone	Muscle	Skin and Hair	Digestive Tract	Liver	Other Viscera
Ca^{45}	22.0	0.33	0.20	0.36	0.12	0.23
Sr^{89}	12.0	0.17	0.15	0.23	0.07	0.13
P^{32}	5.2	1.4	0.75	1.3	3.0	2.1

shows autoradiographs of two mice carrying bilateral subcutaneous lymphosarcomata which were sacrificed and sectioned following radio-phosphorus (right) and radio-strontium (left) administration. In the case of phosphorus, there has been marked concentration of these atoms in the subcutaneous tumors, in addition to their deposition in other soft tissues and the skeleton. But on the left it is seen that the strontium deposition is almost completely limited to the skeletal structure, without deposition in the tumors or other soft tissues. Again it must be emphasized that strontium here acts like calcium; it has been used in these studies because of the difficulty of making adequate quantities of radioactive calcium.

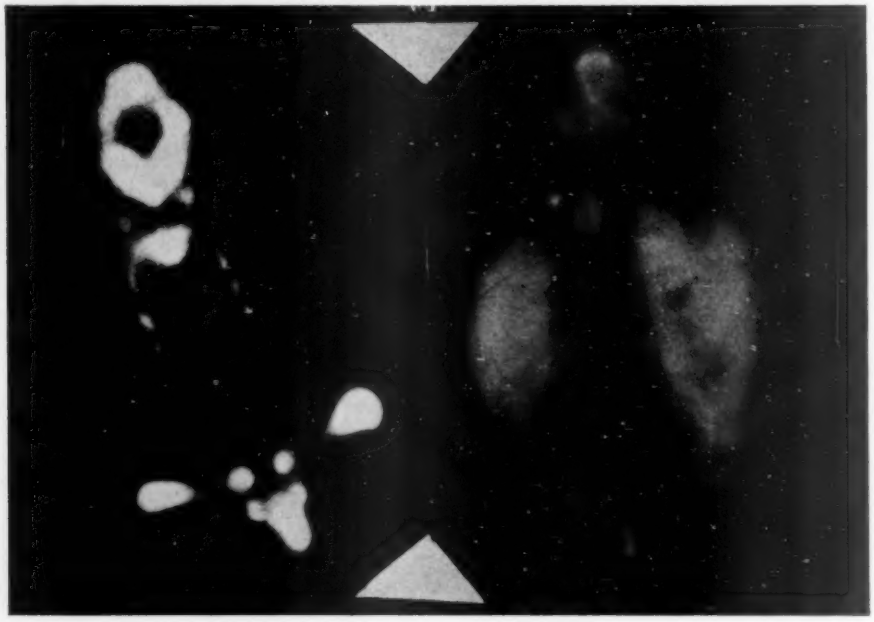

FIG. 6. Autoradiographs of two mice carrying subcutaneous bilateral lymphosarcomata, and given sodium radio-phosphate (*right*) and radio-strontium lactate (*left*) five days before being sacrificed. The selective deposition of strontium in bone and phosphorus in the neoplastic cells is visually demonstrated.

The selective deposition of certain of these elements in specific tissues has led to the use of some of them, especially phosphorus and strontium, in the treatment of hyperplastic or neoplastic diseases limited to those tissues. In leukemia in human beings as well as in animals the uptake of phosphorus is the greatest in those tissues which have leukemic infiltration.[6,21,24,32] Therefore, it is possible to treat this group of patients with some success by the administration of relatively large doses of radioactive phosphorus, whereby the involved areas are selectively irradiated. Figure 7 shows a typical hematological reaction to this form of therapy with the falling white count and the rising red count. At the present time, small weekly or semi-weekly doses are given intravenously over a period of four to eight weeks, so that the patient receives about 2 r whole body irradiation per twenty-four hour period during this time. This dosage does no damage to the red blood cell mechanism and gives excellent responses in cases of chronic myelogenous and chronic lymphatic leukemia. Figure 8 demonstrates this plan of treatment. The actual activity in millicuries in the body is plotted against time. Four years' experience in the thera-

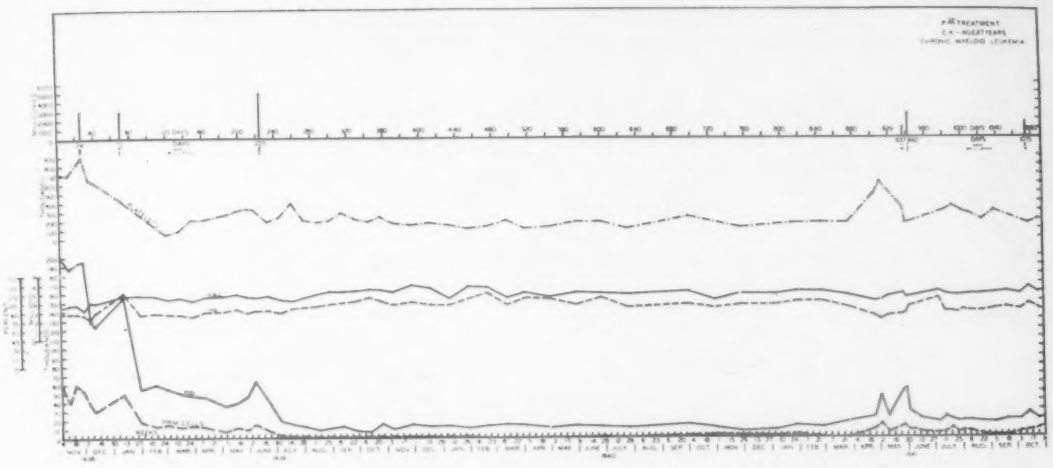

FIG. 7. Hematological response in chronic myelogenous leukemia after therapy with sodium radio-phosphate. During a period of four years six doses were administered as indicated in the top line. Clinically the patient has been relieved of symptoms and has carried on his normal activities.

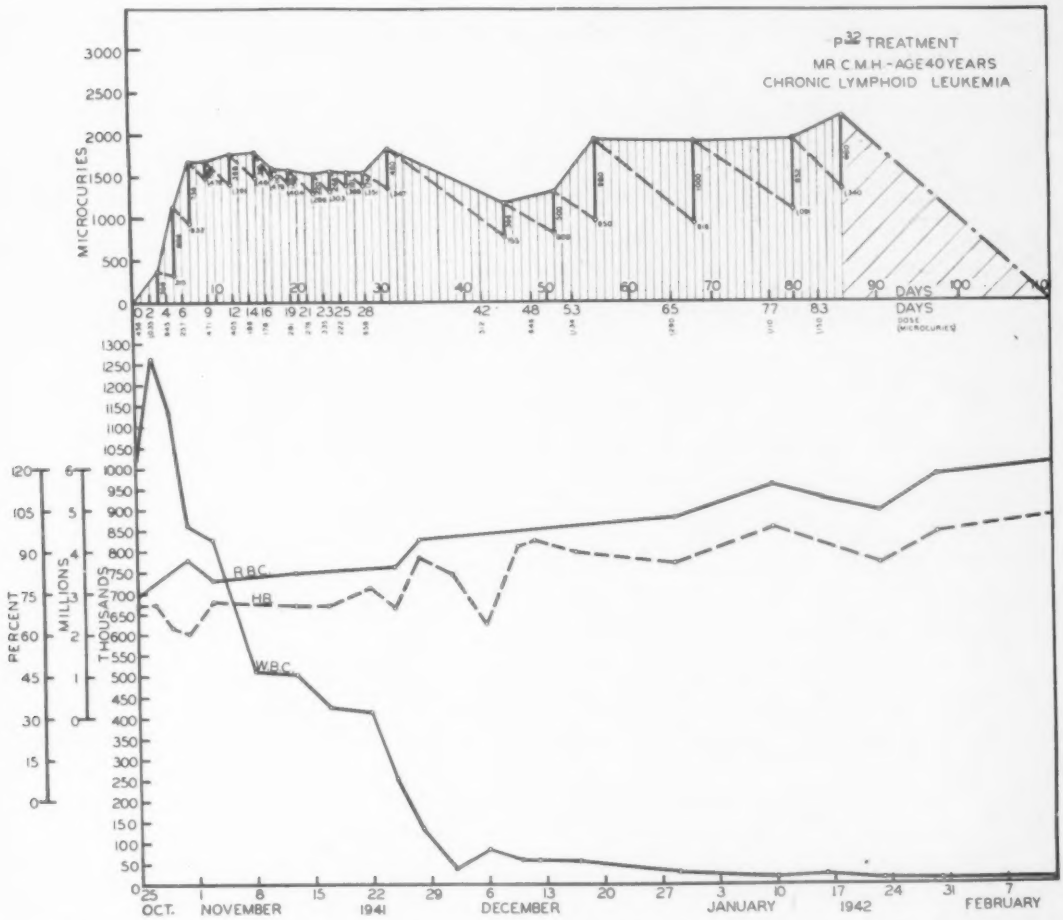

FIG. 8. Hematological response to radio-phosphorus in a patient with leukemia. At the top are plotted the actual activities of P^{32} in the body, at various periods, and after correcting for excretion and decay. The radio-phosphorus in the form of sodium phosphate was given intravenously every few days as indicated.

peutic use of P^{32} allows us to draw the following conclusions: The results apparently are as good as those with roentgen irradiation in prolonging the comfortable life of the patient; the immediate responses to therapy are very satisfactory; and the greatest advantage over roentgen irradiation seems to be the absence of irradiation sickness and reactions. The degree of prolongation of life must await longer observation of the patients already treated. Table v summarizes the results obtained so far.

In different experimental tumors in animals as well as in lymphosarcoma in patients, it has been found that tumor tissue, particularly lymphosarcoma, takes up more phosphorus per gram of weight than any other tissue except bone and bone marrow. Consequently in widespread and metastatic tumors of various kinds, radio-phosphorus has been and is being used therapeutically with encouraging results. Of course, the chief difficulty here is that ten days after the administration of phosphorus the uptake in bone and bone marrow is higher than in any other tissue, and therefore the limiting factor in the use of radioactive phosphorus in metastatic cancer is its effect on the bone marrow which may result in a leukopenia. In order to prevent such an outcome the dosage must be kept relatively

TABLE V

PREVIOUSLY UNTREATED CHRONIC LEUKEMIA
1938–1942

	Myeloid		Lymphoid	
	Number of cases	Per Cent	Number of Cases	Per Cent
Total	21		18	
Now living	16	76.2	9	50.0
Survival after start of P^{32}				
Less than 3 mos.	5 (3 dead)	23.8	4 (3 dead)	22.2
3–6 mos.	1	4.7	4 (4 dead)	22.2
6–12 mos.	3	14.3	4 (1 dead)	16.3
12–18 mos.	6 (2 dead)	28.6	4 (2 dead)	22.2
18–24 mos.	3	14.3	0	
over 24 mos.	3	14.3	3 (1 dead)	16.6
AVERAGE PERIOD OF OBSERVATION	13.5 mos.		11.4 mos.	
REMISSIONS*				
1. Complete	11	52.4	5	27.8
Longest duration	19.0 mos. (1 case)		31.0 mos. (1 case)	
Shortest duration	1.0 mos. (1 case)		3.0 mos. (1 case)	
Average duration	7.6 mos.		12.6 mos.	
2. Partial	11	52.4	4	22.2
Longest duration	12.0 mos. (1 case)		12.0 mos. (2 cases)	
Shortest duration	1.0 mos. (1 case)		6.0 mos. (1 case)	
Average duration	5.2 mos.		10.0 mos.	
3. No remissions to date	4 (4 dead)	19.0	10** (9 dead)	55.5

* more than one remission in some cases

** 1 case under treatment 2 months.

A summary of the results of treatment of chronic lymphatic and myelogenous leukemia with radio-phosphorus. None of the patients had received any treatment prior to therapy with radio-phosphorus.

low. The most encouraging results have been obtained in the treatment of generalized lymphosarcoma, which, as we all know, is a very radiosensitive disease. In many of the patients treated complete regressions have occurred, but whether or not these regressions will be permanent cannot be stated at present. The extreme radiosensitivity of lymphosarcoma generally and the tendency of the disease to disappear temporarily make one cautious in drawing any conclusions regarding the effectiveness of this new form of therapy. The same technique of frequent small doses is now being used. With doses similar in size and frequency to those used in leukemia, there is no fall in the number of white blood cells. Apparently the rapidly growing cells, i.e., the white blood cells in leukemia, the red blood cells in polycythemia (see below) and the tumor cells in lymphosarcoma, are reduced in number by quantities of radiation which do not affect their normal analogues.

In the study of several cases of Hodgkin's disease, in which tracer doses of radioactive phosphorus were administered before death, the uptake of phosphorus in the diseased tissue was not very high.[7] Therapeutic trials in over 30 patients have shown that phosphorus probably will not be very effective in the treatment of Hodgkin's disease. However, we are still using it in repeated small doses. In general, the plan is to give the patient weekly doses over a period of six to eight weeks, thus giving continuous whole body irradiation.

Since radioactive phosphorus tends to concentrate in the bone marrow, it is also being used with success in controlling polycythemia vera.[8] By giving relatively small doses of radioactive phosphorus, the production of red blood cells is slowed down with complete relief of symptoms and satisfactory control of the condition. Figure 9 shows the typical hematological response in a patient with polycythemia. Although the red blood cells have fallen, there has been no decrease in the leukocytes. To date 20 patients have been treated, and in all instances the red cells have fallen to normal levels after small doses. Many of the patients have gone for many months before a second course of therapy was necessary. Table VI summarizes the results.

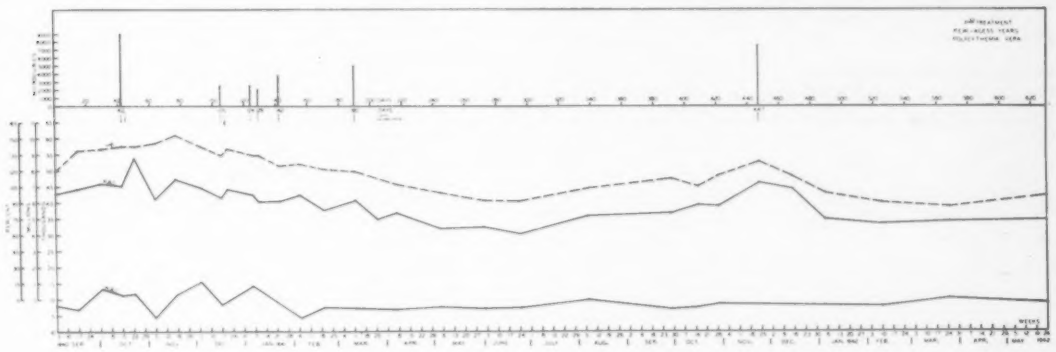

Fig. 9. Hematological response to radio-phosphorus in a patient with polycythemia vera showing the return of the red count and hemoglobin to normal values.

We have discussed the localization of strontium in bone. During the past year considerable clinical investigation has been carried on with radioactive strontium. At the present time a series of cases of metastatic cancer of the breast to the bone and of metastatic cancer of the prostate to bone are being treated. Table VII shows the distribution of strontium in the tissues of a patient, dying from generalized carcinomatosis, primary in the breast. There was extensive involvement of the skeleton and the patient was given a "tracer" dose

TABLE VI

SUMMARY OF THERAPEUTIC RESULTS OF THE USE OF RADIO-PHOSPHORUS IN THE TREATMENT OF POLYCYTHEMIA VERA

	Number of Cases		Per Cent
Total cases	19		
Now living	19		100.0
REMISSIONS			
1. Complete	8		42.1
Longest duration		27.0 mos. (1 case)	
Shortest duration		1.0 mo. (1 case)	
Average duration		11.3 mos.	
2. Partial (Duration 1–6 mos.)	3		15.8
3. No remission to date*	8		42.1
AVERAGE PERIOD OF OBSERVATION		10.0 mos.	
Longest period of observation		29.0 mos. (2 cases)	
Shortest period of observation		1.0 mo. (3 cases)	

* 3 cases under treatment—1 mo.
2 cases under treatment—2 mos.
1 case under treatment—3 mos.

of strontium lactate three days before death. The uptake in involved bone was very high while that in the soft tissues was practically nil. Some of the results in one of the treated patients, a doctor with metastatic prostatic bone cancer (the primary lesion was controlled by roentgen irradiation) are shown in Figure 10. Among these are return of the serum phosphatase values to normal and the fall in the red blood count due to the irradiation as well as associated cessation of progression of roentgen-ray changes and control of pain. After discontinuing the treatment with strontium the red blood cells returned to normal. It is too early to evaluate this form of therapy, but the results so far are encouraging enough to warrant further investigation.

Some other therapeutic attempts and metabolic studies are being made with strontium in osteogenic sarcoma.[31] Associated with the high phosphatase activity of osteogenic sarcoma tissue, the uptake of phosphorus atoms, calcium atoms, and strontium atoms is high. In Table VIII are listed the results of assay of osteogenic sarcoma and surrounding normal tissues removed at biopsy from a patient previously given a tracer dose of radioactive strontium. The uptake of strontium atoms by the osteogenic sarcoma tissue is relatively high. These observations suggest that radioactive strontium may be useful in the treatment of osteogenic sarcoma. However, the high radioresistance of this type of tumor reduces the possibilities of success. In 5 cases studied this selective uptake was observed. Figure 11 shows an autoradiograph

TABLE VII

DISTRIBUTION OF RADIOACTIVE STRONTIUM THREE DAYS AFTER ADMINISTRATION OF 0.3 MILLICURIE OF RADIOACTIVE STRONTIUM LACTATE

S.M. Female, 53 (breast carcinoma with multiple bone metastases)

Fat	0.00018	Stomach	0.00103
Liver	0.00058	Endocardium	0.00133
Brain	0.00067	Small intestine	0.00133
Heart	0.00069	Large intestine	0.00312
Spleen	0.00073	Aorta	0.00339
Tumor breast	0.00075	Sternal cartilage	0.029
Metastasis liver	0.00077	Whole rib	0.057
Muscle	0.00078	Bone (head femur)	0.140
Lung	0.00090	Bone (head femur)	0.159
Kidney	0.00099	Bone (femur shaft)	0.209

Microcuries per gram wet weight

TABLE VIII

DISTRIBUTION OF RADIO-STRONTIUM IN TISSUES FROM A PATIENT (W.L.) WITH OSTEOGENIC SARCOMA OF THE HIP

1.462 mc. radioactive strontium administered intravenously 5/20/41

Biopsy taken: 5/29/41
Tissues assayed: 6/2/41

TISSUE	RADIO-STRONTIUM UPTAKE PER GRAM TISSUE	PERCENTAGE OF DOSE PER GRAM TISSUE
Bone (infiltrated)	0.498 microcuries	0.034
Tumor	0.361 microcuries	0.0246
Skin (normal)	0.342 microcuries	0.0223
Bone (apparently uninvolved)	0.244 microcuries	0.0166
Bone and marrow	0.1948 microcuries	0.0131
Muscle (normal?)	0.1475 microcuries	0.0100
Blood clot	0.0684 microcuries	0.0046
Fat	0.0066 microcuries	0.0004

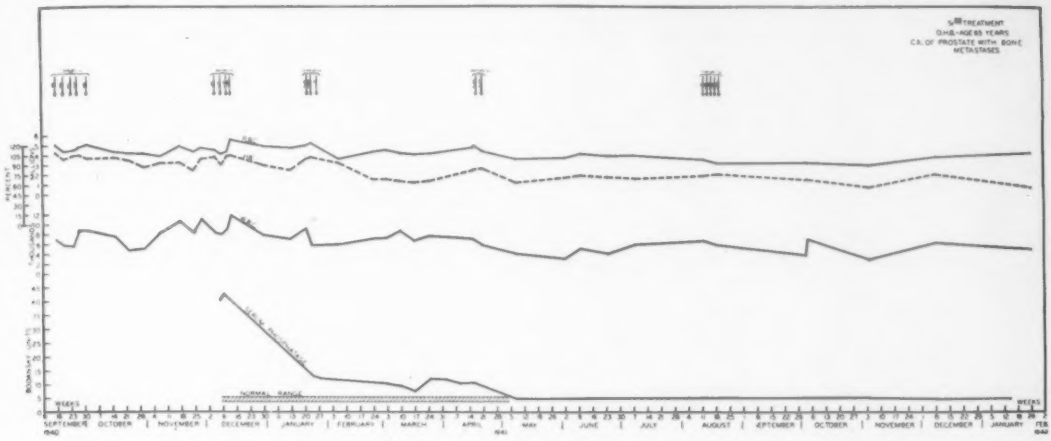

Fig. 10. A summary of the hematological and serum phosphatase changes in a patient with metastatic prostatic cancer of bone following the intravenous administration of radio-strontium as strontium lactate. Notations at top of chart indicate date of administration and amount of radio-strontium given.

of one of these cases in which the amputated limb was sectioned and placed against the photographic film and allowed to remain there for several hours, followed by development of the film. Again the concentration of the strontium atoms is noted in the neoplastic tissue and along the epiphyseal line, where growth is taking place.

To Summarize: In therapeutic work, four elements or compounds are now being used. These are radioactive strontium, radioactive phosphorus, chromic radio-phosphate, and radioactive iodine. We believe that many other elements will find application, particularly if they can be attached to a dye or to an organic compound which might selectively localize in cancerous tissue. Since there are over two hundred radioactive elements available, only a beginning has been made; there is much room for investigation along this line.

Finally, I should like to discuss briefly the biological and medical work that has been carried out with neutron rays. As pointed out previously, these new particles which are produced in the cyclotron by the bombardment of a beryllium target with high speed deuterons have the property of penetrating into tissue rather deeply, somewhat similar in degree to high voltage roentgen rays. In contrast to roentgen rays or gamma rays, which are wave-like, these neutron rays are particulate and produce their biological effects in tissue by striking especially the nuclei of

Fig. 11. Roentgenogram (*left*) and autoradiograph (*right*) of section of amputated leg from patient previously given radio-strontium lactate. The uptake of strontium by the tumor and at the epiphyseal line is to be noted.

TABLE IX

COMPARATIVE EFFECTS OF NEUTRONS AND X-RAYS

Worker	Biological Material	Process Studied	I Exposures of X-rays r	II Exposures of Neutrons n	III Ratios of Exposures r/n	IV Ratios of Tissue Doses, $\left(\frac{\text{x or Gamma}}{\text{Neutrons}}\right)$
Axelrod *et al.* (18)	Mouse tumors *in vitro*	Inhibition of growth				
	Lympho-sarcoma		2,450	325	7.5	3.0
	Lymphoma		1,700	290	5.8	2.3
	Mammary carcinoma		3,250	525	6.1	2.45
Axelrod (19)	Bacteriophage (staphylococcus)	Inactivation	20,000	11,000	1.8	0.72
Spear *et al.* (20)	*E. Coli*	Lethal effect			3.2	1.28
	Mesentericus spores	Lethal effect			5.3	2.1
Dempster (21)	*Drosophila melanogaster* (mutations)	Recessive linked lethal mutations			1.9	0.75
		Gross translocations			3.1	1.24
		Dominant lethal mutations			3.8	1.51
Gray *et al.* (22)	Bean roots				(77)	11.0
	Chick fibroblasts (in tissue culture)				(11.5 to 22.5)	2.1 to 3.2
Lewis (23)	Chick embryo Fibroblasts (in tissue culture)	Inhibition of growth	110,000	55,000	2.0	0.8
Marshak (24)	Horsebean	Per cent abnormal mitosis	65	10	6.5	2.6
	Pea	Per cent abnormal mitosis	205	33	6.2	2.5
	Tomato	Per cent abnormal mitosis	1,235	190	6.5	2.6
	Mouse sarcoma 180	Per cent abnormal mitosis	765	130	5.8	2.3
	Mammary carcinoma					
	Lymphoma					
Zirkle & Lampe (25)	*Drosophila* eggs	Inhibition of hatching by 50 per cent				
	$1\frac{1}{2}$ hours		150	79	1.9	0.76
	$4\frac{1}{2}$ hours		745	240	3.1	1.24
	6 hours		785	290	2.7	1.08
	Wheat seedlings	Inhibition of growth of:				
		root			6.2 to 11.8	2.5 to 4.7
		shoot			5.9 to 9	2.4 to 3.6

Summary of the comparative effects of neutrons and roentgen rays upon different biological systems (from Aebersold and Lawrence).[1]

hydrogen atoms which are driven into the tissue and cause proton ionization, as contrasted with electron ionization produced in tissues when they are bombarded by gamma rays and roentgen rays. Neutron ionization in tissue is very dense as compared to the ionization produced by roentgen rays or gamma rays. For this reason it was suspected that the biological effects of neutrons would be considerably different from those of roentgen rays or gamma rays, and indeed this has been found to be true. Figure 12 shows the reaction that takes place when neutrons are produced in the cyclotron. In Figure 13, the differences in the characteristics of the ionization produced by neutrons and roentgen rays are seen. It is a Wilson cloud chamber photograph of hydrogen being bombarded by a mixture of gamma rays and fast neutron rays. The very wide, long tracks represent the ionization produced by proton recoil atoms and the fine tracks in the background represent electrons secondary to gamma-ray bombardment. The marked difference in the density of the ions formed along these tracks can be seen. Table IX summarizes the biological investigations carried on in comparing neutrons and roentgen rays.[1] The varying ratios confirm the suspected difference in the biological effects of these two forms of radiation; that is, that some tissues are affected more than others by neutron rays. For this reason neutron rays immediately assumed clinical interest and it seemed important to exhaust their possibilities in the treatment of cancer. For two and a half years under the direction of

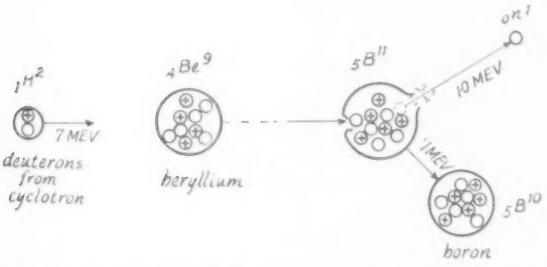

Fig. 12. A diagrammatic representation of the production of neutrons by the bombardment of beryllium with high speed deuterons.

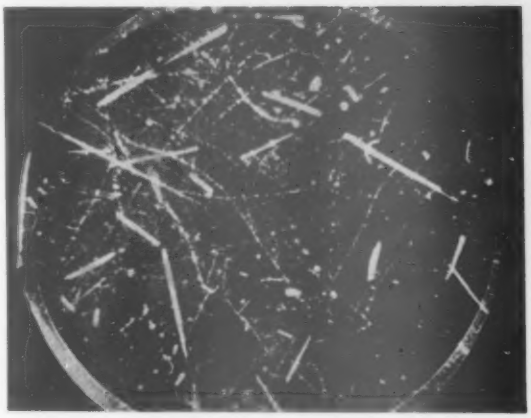

Fig. 13. Ionization produced in a Wilson cloud chamber filled with a mixture of air, hydrogen and water vapor after bombardment with neutron rays and gamma rays from the cyclotron. The thin tracks of ions were produced by secondary electrons liberated by the gamma rays, while the thick and very dense tracks were produced by the recoil protons resulting from collisions of neutrons with the hydrogen atomic nuclei. This illustration demonstrates the more localized and intense ionization produced in tissues by neutrons when compared with roentgen rays or gamma rays.

Dr. Robert S. Stone with his associate Dr. John C. Larkin, clinical trials have been and are being carried out with direct neutron radiation. Tri-weekly treatments for varying periods of time are given by methods similar to those used in protracted roentgen treatment. The results are encouraging, but perhaps a few years will elapse before the final picture is clear. Most of the patients treated have been those with advanced incurable cancer. Even in this group, the results have been favorable enough to indicate that the therapeutic value of direct neutron irradiation must be exhaustively investigated.[29]

The study of the artificial radioactive substances and of neutron rays in therapy is a fruitful field. Much work must be done, but the future is very encouraging. The preliminary studies have given favorable results. It is certain that these new radioelements and neutrons will take their place along with radium, roentgen rays, and surgery in the treatment of cancer and allied diseases. Shortly after the discovery of

radium, Sir Joseph Thomson, speaking as President of the British Association for the Advancement of Science at Winnipeg said, "The physiological and medical properties of the rays emitted by radium is a field of research in which enough has already been done to justify the hope that it may lead to considerable alleviation of human suffering. It seems quite definitely established that for some diseases, notably rodent ulcer, treatment with these rays has produced remarkable cures; it is imperative lest we should be passing over a means of saving life and health, that the subject should be investigated in a much more systematic and extensive manner than there has yet been either time or material for." These predictions of Sir Joseph Thomson have certainly come true as pioneered by such martyrs as Dr. Eugene Wilson Caldwell, and attested by the work of the members of this Society. Today investigators are at about the same point in the development of this new field as was Dr. Caldwell and others in 1905 in the development of roentgen rays and radium. If Sir Joseph were alive today, he undoubtedly would make the same statements and predictions concerning artificial radioactivity. In the field of artificial radioactivity, however, we have not only one element, as in the case of radium, but actually one or more isotopes for each chemical element, which fact multiplies the possible biological and medical applications. Therefore, their value as therapeutic agents must be carefully and extensively investigated.

To Summarize: The physicist has given a two-edged sword to the biologist and medical investigator. Artificial radioactivity provides: first, a method of labelling atoms for studies in metabolism, and second, a substitute for radium in the treatment of disease based on selective localization of the various elements. It seems probable that in the future radioactive isotopes and the Geiger counter will be as necessary a part of the armamentarium of the biologist as is the microscope at the present time. The contributions of the new nuclear physics to biology and medicine emphasize again the fact that undreamed-of practical applications often result from fundamental discoveries.

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THE GASTROINTESTINAL TRACT IN THE HEALTHY NEWBORN INFANT*

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PROBABLY no other group of individuals so nearly approaches the healthy state as do newborn infants. Consequently in the investigation of the normal anatomy and physiology of any organ or group of organs it seems fitting to begin with these young subjects. This is particularly so in the case of the gastrointestinal tract. In most studies of normal as well as of diseased individuals the roentgen examination must usually play a highly important part, and nowhere is this more true than in the investigation of the alimentary canal.

Before proceeding with a discussion of the roentgen examination of the newborn infant it seems advisable to consider in some detail, first, the embryology, and second, the fetal physiology of the digestive tract. The material for the section on embryology has been obtained from Arey,[1] Frazer,[8] Hooker,[10] and Jordan and Kindred.[12]

EMBRYOLOGY OF THE GASTROINTESTINAL TRACT

Origin of the Alimentary Canal. Very early in embryonic life the individual to be consists of a flat disc which rests upon the yolk sac or umbilical vesicle. The alimentary tract originally is a relatively straight tube. This tube develops from that part of the vault of the yolk sac which is under the embryonic disc. The embryo or embryonic disc becomes pinched off from the yolk sac by three grooves or sulci. Dorsal portions of the sac are included along with the embryo in this process. A closed anterior or cephalic portion forms the foregut, from which the esophagus, stomach and probably a part of the duodenum develop. The mid-dorsal or temporarily open portion of the yolk sac in this constricting process becomes the midgut, while a closed posterior or caudal portion becomes the hindgut. The midgut and hindgut develop into the small and large intestine.

The Two Primary Layers of the Digestive Tract. The gastrointestinal tract is composed of an inner lining or tube of entoderm. This is the primary tissue which develops into the mucosa, including the glandular ingrowths. Splanchnic mesoderm forms the outer or covering layer and from it are developed surface peritoneum, muscle and connective tissue. The lining epithelium becomes thicker by proliferation. There are stages in the growth of all parts of the gut, but particularly in that of the esophagus and duodenum in which temporary occlusion of the lumen occurs due to rapid cellular proliferation. Later there occurs a normal process of recanalization of the digestive tube, but congenital stenosis or complete atresia may occasionally result from failure of re-establishment of a lumen. The lining layer develops faster than the covering layer of the tract, and hence, folds or rugae are formed. By the seventh week, the circular muscle layer has developed, while the longitudinal layer does not develop until the twelfth week.

The Pharyngeal and Anal Membranes. The digestive tube establishes communication with the exterior through rupture of the pharyngeal membrane and of the anal membrane. The pharyngeal membrane is the floor of a shallow depression external to the cephalic end of the primitive foregut, known as the stomodeum. The proctodeum is the name for a similar shallow depression external to the caudal end of the hindgut, and the floor of the proctodeum constitutes the anal membrane. Rupture of the pharyngeal membrane occurs at the 3 mm. stage of embryonic development while the anal membrane does not rupture until the 25 mm. stage.

Esophagus. The esophagus, derived from the cephalic portion of the foregut, at four weeks appears as a straight tube leading from the pharynx to the stomach. Growth in length is rapid. Irregular channeling of the lumen occurs as a result of rapid epithelial proliferation.

Stomach. At the 4 mm. stage of embryonic life the future stomach appears as a spindle-shaped or fusiform enlargement of the foregut.

*Read at the Forty-second Annual Meeting, American Roentgen Ray Society, Cincinnati, Ohio, Sept. 23–26, 1941.

While it is originally in high position, forward growth of the cephalic end of the embryo results by the seventh week in a "descent" to its adult location. During the "descent" it undergoes a double rotation due largely to unequal growth, greater in its original dorsal and sinistral walls, less in its original ventral and dextral walls. That the rotation of the stomach is a fact is proved by the distribution of the vagus nerves —the right to the dorsal wall of the adult stomach, the left to the ventral wall. When rotation is completed the original ventral border has become the lesser curvature, lying toward the right and upward, while the eventual greater curvature, that is, the whole of the sinistral-caudal border of the adult stomach is derived from the original dorsal wall.

The Intestine. At the 5 mm. stage (four week embryo) the intestine is a simple tube, with a ventral bend in the sagittal plane, extending from the stomach to the anal membrane. The duodenum can be seen at this stage as distinct from the remainder of the intestine. About the 9 mm. stage the intestinal loop becomes flexed anteriorly. The attachment between the yolk stalk and the intestine is probably continued beyond this time, although the lumen connection between the two is usually no longer present. The cecum now appears as a bulge to indicate the demarcation between the small and large intestine, resulting in a cranial and a caudal limb. Counterclockwise rotation occurs about the superior mesenteric artery as an axis, the caudal limb moving to the left and upward.

Growth of the small intestine now becomes so rapid that for awhile the belly cavity can no longer contain it, and at seven weeks the small intestine and a part of the large bowel escape into the umbilical cord. Here rapid growth continues and the small intestine develops into six primary loops or coils. At ten weeks the belly cavity is again large enough to contain the intestine, the small bowel returning first.

Both small and large intestine occupy the left side of the abdomen at this time. The colic valve results from a sharp U-shaped bend which takes place at ten weeks between the cecum and future ascending colon.

After the primitive colon has become differentiated the cecum gradually moves from its original location in the left lower abdominal cavity to its adult position. As the large intestine then continues to grow the cecum is pushed caudally on the right side, and the ascending colon is established. During this growth of the colon in length the sigmoid flexure is carried medially and downward and the descending colon is thus formed. The appendix up to the fifth month grows equally with the cecum, but thereafter its growth is very slow, while the cecum continues to enlarge. Subdivision of the cloaca results in formation of the rectum. As above noted, the anal membrane ruptures at the 25 mm. stage (approximately the eighth week). Arey[1] says that when this occurs a short ectodermal proctodeum is added to the enterodermal rectum, forming the anal canal.

The intestinal glands of Lieberkühn are said by Arey[1] to first appear toward the end of the third month. They are soon followed by the compound duodenal glands of Brunner, and at five months lymph nodules and Peyer's patches appear.

PHYSIOLOGY OF THE FETAL DIGESTIVE SYSTEM

It has been established with reasonable certainty that the digestive tract of the fetus begins to function early in fetal life. Among the functions which have been shown to occur at some time before birth are: (1) the act of swallowing; (2) gastric peristalsis and motility; (3) hunger contractions of the stomach; (4) peristalsis of the intestines with intestinal motility, and (5) absorption from the intestinal tract.

Windle[25] says that Preyer expressed the opinion held as early as 1885 in the statement: "That amniotic fluid is a food for the fetus is certain but if it is not swallowed plentifully it contributes little to nourishment beyond mere water feeding." Menees, Miller and Holly[16] injected a one to one solution of strontium iodide through the anterior abdominal wall into the amniotic sac. They found a shadow in the region of the left costal margin of the fetus in a large percentage of roentgenograms made some time after the injections. This was interpreted as strontium iodide in the fetal stomach, and they concluded that the swallowing of amniotic fluid must occur frequently. Windle reviews the findings of Ehrhardt who injected "thorotrast" into the amniotic sac of women who were five to six months pregnant. Fifteen hours or more following the injection hysterectomy

was performed. Roentgenograms of the uterus and its contents revealed very clear shadows of the fetal stomach. Becker, Windle, Barth and Schulz[2] worked with guinea pigs and found that under normal physiological conditions in utero the fetus begins to swallow amniotic fluid about the forty-second day of gestation. They used 0.4 to 1.0 cc. of colloidal thorium hydroxide or dioxide for injection into the amniotic sac and then made roentgenograms at varying intervals. The time taken for the contrast medium to reach the stomach after injection decreased rapidly with age. Likewise, the opaque material was propelled through the gastrointestinal tract much more rapidly as the fetus became older. Swallowing of amniotic fluid appeared to be enhanced by anoxemia. The swallowing act appeared to begin about the time the fetus began to grow most rapidly. Very recently Hooker[10] examined a fetus of fifteen and one-half weeks. The stomach was found to be filled with amniotic fluid, presumably swallowed by the fetus.

Carlson and Ginsburg[4] made observations on a number of newborn infants and on two pups born eight to ten days before term. The empty stomach at birth and in the prematurely born was found to have the typical periods of tonus and hunger contractions of the adult. They concluded that in the normal mammal the gastric hunger mechanism is completed physiologically and is probably active at some time prior to birth.

Windle and Bishop[26] were able to see "spontaneous" intestinal movements in 35 mm. cat fetuses. The strength of these movements increased rapidly from this time on and by the time the fetus had reached the 70 mm. stage (18 grams) the intestine behaved similarly to that of the unanesthetized kitten (110–120 grams) one or two days after birth. The studies of Yanase on intestinal movements in freshly killed fetuses of the guinea pig and human are reviewed by Windle.[25] Yanase is said to have seen the earliest peristalsis in guinea pigs on about the twenty-sixth or twenty-seventh day of fetal life, at which time the longitudinal muscle of the intestine had been formed. Prior to this time only circular muscle was present, and Yanase obtained merely local constrictions by pinching and by faradic stimulation. Although longitudinal muscle and its nerves could be found in human fetuses after the seventh week, peristalsis was not seen before the eleventh week. However, during the sixth week when circular muscle alone was present local contractions could be obtained in human fetal intestine by faradic stimulation.

Windle[25] found that intestinal peristalsis of the digestive type was associated with segmentation and propagation of intestinal contents. Occasionally a spastic form of rhythmical segmentation of the intestine replaced the usual digestive type of movement. This was more apt to occur under conditions of anoxemia.

It has been found that much of the absorption of amniotic fluid takes place in the fetal stomach (Windle).[25] The small and large bowel retain their contents for relatively long periods during fetal life and it is probable that here likewise much absorption occurs. Although the full significance of fetal swallowing, gastrointestinal movements and absorption is not clear, Windle believes that the absorbed water may be of real use to the fetus.

Arey[1] states that meconium begins to collect in the intestine after the third month. It is a pasty mixture of mucus, bile, cast off epithelial cells and lanugo and vernix caseosa which has been swallowed with amniotic fluid. Windle[25] says that late in fetal life the guinea pig evacuates meconium into the amniotic sac and this is then swallowed with amniotic fluid and again reevacuated. This process has not been demonstrated in the human fetus.

ROENTGENOLOGICAL CONSIDERATIONS

During the past eighteen months roentgen studies have been made on an unselected group of healthy newborn infants. None of these infants had any obvious

physical defects, but in the mothers of 4 the serological examinations were positive; 2 mothers had previously been treated for syphilis, and in 9 cases the maternal serology was not recorded. Three mothers had some degree of arterial hypertension. In 3 cases one or more loops of cord were found about the infant's neck at delivery, in 1 infant the cord was prolapsed, with some fetal distress, and in 1 case there was cephalopelvic disproportion with some difficulty in delivery.

It is evident that in order to draw any conclusions from work of this sort a sufficient number of cases must be observed. This paper deals with the study of 110 patients. Of this number routine gastrointestinal examinations were made on all. In 50 a special small intestine study was made in addition to the usual investigation. There were 59 white and 51 colored babies. Sixty-four were females, while the males numbered 46. Three babies were born at the end of eight to eight and a half months gestation, 1, at seven and a half to eight months, and there was no record as to the term of gestation in 10. The others were full term infants. The age at the time of the examination varied between two and nine days. Only 3 were over one week old when first seen. Birth weights varied from 5 pounds, 8 ounces (2,500 grams) to 9 pounds, 7 ounces (4,275 grams). Full details on these infants, including roentgen findings, are given in Table 1.

METHOD OF PROCEDURE

Nothing is permitted by mouth after 2 A.M. At 8 A.M. a barium meal consisting of a 2 ounce mixture is given, usually from a nursing bottle. A roentgenoscopic study is made immediately after completion of the meal. Following the routine chest survey an additional amount of barium mixture is given for visualization of the esophagus, the baby being prone and rotated toward its right side. The stomach, small intestine and colon are examined roentgenoscopically and by films.

Roentgenograms of the barium-filled stomach are made with the infant prone, followed by anteroposterior and lateral views in the erect position. In the routine gastrointestinal examinations roentgenoscopic studies are then made every two hours until the stomach is empty, or up to the end of eight hours. At this time the infant is returned to its usual milk formula, but the examinations are made every day thereafter until the stomach and intestinal tract are empty of the barium. In those cases in which special small bowel studies are performed, a follow-up roentgenogram of the abdomen is made every hour up to the end of eight hours, with frequent roentgenoscopic surveys.

It has been difficult to compare the findings of others with those of the present study. In many instances the statement appears that roentgen examinations were made on infants, but no information is given concerning the actual ages of the patients. In other papers reports have been made on the collective findings of both infants and children. As far as can be determined from an incomplete survey of the literature very little work of this nature has been done previously on newborn infants alone.

Bouslog, Cunningham, Hanner, Walton and Waltz[3] made roentgen examinations of the gastrointestinal tract in a group of 133 infants, ranging in age from one week to six months. Regular feedings were continued in this group at four hour intervals which made determination of the emptying time of the stomach a difficult matter. However, in a special series of 10 infants feedings were withheld until the stomach was empty. Three of this special group were studied roentgenoscopically and by films, while the others were examined by roentgenograms made in semi-oblique prone position. The esophagus was not studied but particular attention was given to the shape, size, position, peristalsis, height of the lower pole, air bubble and emptying time of the stomach. In the special group of 10 the emptying time was found to vary between three and eight hours. However, in the

Table I

MASTER TABLE GIVING DATA ON THE EXAMINATIONS OF THE GASTROINTESTINAL TRACT IN A GROUP OF 110 NEWBORN INFANTS; ARRANGEMENT ACCORDING TO TYPE OF MEAL USED

Newborn Number	Age in days	Color	Sex	Full term	Maternal serology	•	Birth weight lb.-oz. / gm.	Complications	Stomach												Special small intestine study
									Type of meal	†	‡	§	Cascading	‖	¶	••	††	Pyloro-spasm	Amount of meal remaining at 8 hr T = Trace; FT = Faint trace; VFT = Very faint trace	Emptying time in hours + after numeral = "more than"; − after numeral = "less than"	
1	5	W	F	Yes	Neg.	PV	7-3 / 3275	Prolapse of cord; fetal distress	Barium sulphate—distilled water	R	L	A	Yes	T 12	O	S-L 1/3	M	No	1/5	8+ 24−	Yes
2	3	B	M	Yes	Neg.	LF	9-1 / 4125	Cephalo pelvic disproportion	"	S H	S	S	Yes	T 11	O	Mod-M 1/3	S	No	1/6	24+ 48−	Yes
3	3	W	M	Yes	Neg.	CS	7-1 / 3200	None	"	S H	M	A	No	L 2	O	S-L 1/3	M	No	1/8	8+ 24−	Yes
4	5	W	F	Yes	Neg.	S	6-7 / 2935	None	"	S H	S	A	No	L 3	O	S-M 1/3	M	No	2/5	24+ 48−	Yes
5	4	W	M	Yes	Neg.	S	6-13 / 3105	None	"	T P	S	S	Yes	T 12	O	Mod-L 1/3	R	No	o	5½	Yes
6	5	W	M	Yes	Neg.	S	7-9 / 3450	None	"	S H	L	S	No	L 3	Ho	D-U 1/3	M	1+	o	7	Yes
7	4	B	F	Yes	Neg. Mother had treatment	S	7-2 / 3225	None	"	S H	S	S	Yes	T 12	O	S-L 1/3	M	No	VFT	8	Yes
8	3	B	F	Yes	Neg.	BD	6-12 / 3050	None	"	F H	L	A	No	L 1	Ho	S-L 1/3	M	No	FT	24+	Yes
9	3	B	F	Yes	Neg.	S	5-10 / 2550	None	"	S H	S	A	No	L 2	O	Mod-U 1/3	S	No	1/4	24+ 48−	Yes
10	3	B	M	Yes	Neg. Wass. 2+ in 1935	S	7-1 / 3200	None	"	S H	M	A	No	L 3	O	S-M 1/3	S	No	T	8+ 24−	Yes
11	4	W	F	Yes	Neg.	S	8-8 / 3875	None	"	S H	L	A	Yes	T 12	O	Mod-M 1/3	M	No	1/4	48+ 72−	Yes
12	5	W	M	Yes	Neg.	S	6− / 2735	None	"	S H	S	A	No	L 1	O	Mod-L 1/3	M	No	1/8	8+ 24−	Yes
13	3	B	F	Yes	Not recorded	S	6-13 / 3075	None	"	S H	S	A	No	L 1	O	S-L 1/3	M	No	1/6	8+ 24−	Yes
14	3	W	F	Yes	Neg.	LF	7-11 / 3480	None	"	S H	S	A	No	L 2	O	S-M 1/3	M	No	FT	8+ 24−	No
15	7	W	F	Yes	Neg.	LF	7-3 / 3250	2 loops of cord around neck	"	S H	M	A	No	L 2	O	S-M 1/3	S	No	o	8	Yes
16	2	W	F	Yes	Neg.	BD	9-9 / 4350	None	"	S H	L	S	No	T 12	Ho	S-L 1/3	M	No	FT	8+ 24−	No
17	4	W	F	Yes	Neg.	S	6-3 / 2825	None	"	S H	L	A	No	L 2	O	S-L 1/3	R	No	o	4+ 8−	Yes
18	3	B	M	Yes	Not recorded	CS	6-8 / 2965	None	"	T P	S	S	Yes	T 12	O	S-L 1/3	R	No	1/8	8+ 24−	

• (Delivery) S = Spontaneous; LF = Low forceps; CS = Cesarean Section; PV = Podalic version; BD = Breech delivery.
† (Shape of Stomach) FH = Fishhook; SH = Steerhorn; R = Retort; TP = Tobacco pouch; Sc = Scaphoid.
‡ (Size of gas bubble) S = Small; M = Medium; L = Large.
§ (Size of stomach) A = Average; S = Small; L = Large.
‖ Position of greater curvature in relation to vertebral level in erect position.
¶ (Tonicity) O = Orthotonic; Ho = Hypotonic; Hr = Hypertonic.
•• (Peristalsis—Character and location of beginning waves) S = Shallow; Mod = Moderate; D = Deep; U = Upper; M = Middle; L = Lower.
†† (Early gastric motility) S = Slow· M = Moderate; R = Rapid.

TABLE I

MASTER TABLE GIVING DATA ON THE EXAMINATIONS OF THE GASTROINTESTINAL TRACT IN A GROUP OF 110 NEWBORN INFANTS; ARRANGEMENT ACCORDING TO TYPE OF MEAL USED

Small Intestine															Colon							
		Continuous Small Bowel Loops						Segmentation of Small Bowel														
		A = Throughout Examination B = Early, that is, during 1st 2 to 3 hr. C = Late, that is, after 1st 2 to 3 hr. 1+ = Slight 2+ = Moderate 3+ = Marked J = Jejunum I = Ileum																			
		A		B		C		A		B		C										
Special small intestine study	Duodenal cap visualized	J	I	J	I	J	I	J	I	J	I	J	I	Time in hours for meal to enter cecum	Location of head of meal in 8 hr.	Appendix visualized	Amount of meal evacuated from colon in 24 hours 0 = None 1+ = Trace only 2+ = Moderate amount 3+ = Marked amount 4+ = Complete						Remarks
																	0	1+	2+	3+	4+	
Yes	Yes			1+			2+	1+			2+	1+	1+	4	Transv. colon	No				x		
Yes	Yes					2+	1+			2+	2+		2+	5	Transv. colon	No					x	
Yes	Yes			3+		2+			3+					4	Splenic flexure	No		x				
Yes	Yes			2+		1+			3+			1+		3½	Splenic flexure	No			x			
Yes	Yes			2+	2+							1+	2+	3½	Sigmoid	No				x		
Yes	Yes			1+	1+							2+	2+	4	Sigmoid	No				x		
Yes	Yes			2+					2+			2+		4	Desc. colon	No				x		
Yes	Yes			2+					2+			2+		4	Desc. colon	No				x		
Yes	Yes			2+			1+		2+					4	Transv. colon	No				x		Unusual late S.I. continuity
Yes	Yes			1+		3+	3+				1+			6	Hepatic flexure	No				x		
Yes	Yes			1+		1+	1+		2+					4	Sigmoid	No				x		
Yes	Yes			3+	2+							1+	2+	5	Sigmoid	No				x		
Yes	Yes					1+	1+			2+	2+	1+	1+	4	Distal tr. colon	No				x		
Yes	Yes			2+	2+							1+	2+	5½	Desc. colon	No				x		
No	Yes												2+	?	Sigmoid	No						
Yes	Yes			2+					3+			2+		3	Evacuated	No					x	
No	Yes													?	Desc. colon	No					x	
Yes	Yes	2+	3+											5	Desc. colon	No			x			

TABLE I—*Continued*

Newborn Number	Age in days	Color	Sex	Full term	Maternal serology	*	Birth weight lb.-oz. / gm.	Complications	Stomach											
									Type of meal	†	‡	§	Cascading	‖	¶	**	††	Pyloro-spasm	Amount of meal remaining at 8 hr. T = Trace; FT = Faint trace; VFT = Very faint trace	Emptying time in hours + after numeral = "more than"; − after numeral = "less than"
19	2	B	F	Yes	1+	S	6-6 / 2880	None	Barium sulphate—distilled water	S H	M	A	No	L 1	O	S-L 1/3	M	No	2/5	48+ 72−
20	3	B	F	Yes	Neg.	S	7 / 3175	None	"	T P	M	A	Yes	T 12	O	S-L 1/3	R	No	1/5	30+
21	7	B	M	Yes	Neg.	S	8-7 / 3825	None	"	T P	M	A	Yes	T 12	Ho	Mod-M 1/3	M	No	0	5
22	3	B	F	Yes	Not recorded	S	6-5 / 2870	None	"	T P	M	A	Yes	T 12	O	S-L 1/3	M	No	1/5	30+
23	3	B	F	Yes	Neg.	S	8-7 / 3825	None	"	S H	S	A	No	L 1	O	Mod-M 1/3	M	No	1/8	72+
24	3	B	M	Yes	Not recorded	CS	6-2 / 2775	None	"	S H	S	S	No	T 11	O	Mod-M 1/3	M	No	1/6	8+ 24−
25	2	B	M	Yes	Neg.	CS	7 / 3175	None	"	T P	S	A	Yes	T 12	O	S-L 1/3	M	No	1/3	8+ 24−
26	7	W	M	Yes	Neg.	S	9-7 / 4295	None	"	S H	S	S	No	L 1	O	S-M 1/3	M	No	0	7
27	7	W	M	Yes	Neg.	S	8-2 / 3695	None	"	R	L	A	Yes	T 12	O	Mod-M 1/3	R	No	FT	24+ 48−
28	3	B	F	Yes	Neg.	S	7-3 / 3200	None	"	T P	S	A	Yes	L 1	O	S-L 1/3	M	No	1/6	8+ 24−
29	5	W	F	Yes	Neg.	S	6-12 / 3055	None	"	S H	S	L	No	L 2	O	S-M 1/3	S	No	FT	8+ 24−
30	3	B	F	Yes	Neg.	S	6-5 / 2875	None	"	T P	M	A	Yes	T 11	O	S-L 1/3	R	No	0	7
31	7	W	F	Yes	Neg.	LF	6-4 / 2825	None	"	F H	M	A	No	L 2	O	S-M 1/3	M	No	1/5	24+ 48−
32	3	B	F	Yes	Not recorded	S	5-11 / 2580	None	"	Sc	M	A	No	L 1	O	Mod-M 1/3	S	No	1/8	8+ 24−
33	4	B	F	Yes	Neg.	S	7-9 / 3450	Hypertension and nephritic toxemia	"	T P	M	S	No	T 12	O	S-M 1/3	S	No	2/5	24+ 48−
34	5	W	M	Yes	Neg.	S	8-1 / 3655	None	"	T P	M	S	No	T 12	O	Mod-M 1/3	M	No	FT	8+ 24−
35	3	B	F	Yes	Neg.	S	7-6 / 3367	None	"	S H	M	A	No	L 1	O	S-L 1/3	S	No	1/3	8+ 24−
36	5	W	F	Yes	Neg.	LF	7-2 / 3215	None	"	S H	S	S	No	T 12	O	S-M 1/3	S	No	0	6
37	6	W	F	Yes	Neg.	LF	6-4 / 2830	None	"	S H	M	A	Yes	L 1	O	Mod-L 1/3	M	No	1/8	8+ 24−

* (Delivery) S = Spontaneous; LF = Low forceps; CS = Cesarean Section; PV = Podalic version; BD = Breech delivery.
† (Shape of Stomach) FH = Fishhook; SH = Steerhorn; R = Retort; TP = Tobacco pouch; Sc = Scaphoid.
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‖ Position of greater curvature in relation to vertebral level in erect position.
¶ (Tonicity) O = Orthotonic; Ho = Hypotonic; Hr = Hypertonic.
** (Peristalsis—Character and location of beginning waves) S = Shallow; Mod = Moderate; D = Deep; U = Upper; M = Middle; L = Lower.
†† (Early gastric motility) S = Slow; M = Moderate; R = Rapid.

TABLE I—*Continued*

Small Intestine															Colon							
		Continuous Small Bowel Loops						Segmentation of Small Bowel									Amount of meal evacuated from colon in 24 hours 0 = None 1+ = Trace only 2+ = Moderate amount 3+ = Marked amount 4+ = Complete						
		A = Throughout Examination B = Early, that is, during 1st 2 to 3 hr. C = Late, that is, after 1st 2 to 3 hr. 1+ = Slight 2+ = Moderate 3+ = Marked J = Jejunum I = Ileum																				
		A		B		C		A		B		C										
Special small intestine study	Duodenal cap visualized	J	I	J	I	J	I	J	I	J	I	J	I	Time in hours for meal to enter cecum	Location of head of meal in 8 hr.	Appendix visualized	0	1+	2+	3+	4+	Remarks
No	Yes			2+									2+	4	Sigmoid	No		x				
No	Yes			1+								1+	2+	?	Transv. colon	No		x				Milk formula at 2½ hours
Yes	Yes				1+			2+					2+	2	Sigmoid	No				x		
No	Yes			1+									2+	?	Sigmoid	No					x	Milk formula at 2½ hours
Yes	Yes			2+	1+								2+	5	Sigmoid	No				x		
Yes	Yes	2+							2+					4	Sigmoid	No				x		
No	Yes			2+									2+	?	Transv. colon	No	x					
Yes	Yes			1+					2+			1+		3½	Rectum	No				x		
Yes	Yes			3+	3+							1+	1+	2½	Sigmoid	No				x		Rapid early gastric motility
Yes	Yes			1+					2+			1+		3	Sigmoid	No				x		
No	Yes			1+	1+								2+	3	Desc. colon	No					x	
Yes	Yes			2+	2+							2+	2+	2	Evacuated 6 hr.	No					x	
Yes	Yes			2+	2+	2+							2+	5½	Sigmoid	No	x					
Yes	Yes							2+	2+					3	Evacuated	No					x	
Yes	Yes					1+	1+	2+	2+				-	6	Hepatic flexure	No				x		
Yes	Yes			1+								1+	2+	5	Desc. colon	No				x		
Yes	Yes							2+	2+					3	Rectum	No				x		
Yes	Yes												2+	?	Transv. colon	No				x		
Yes	Yes			1+					1+					3	Sigmoid	No		x				

TABLE I—*Continued*

Newborn Number	Age in days	Color	Sex	Full term	Maternal serology	*	Birth weight lb.-oz. / gm.	Complications	Stomach											
									Type of meal	†	‡	§	Cascading	‖	¶	**	††	Pyloro-spasm	Amount of meal remaining at 8 hr. T = Trace; FT = Faint trace; VFT = Very faint trace	Emptying time in hours + after numeral = "more than"; − after numeral = "less than"
38	6	W	F	Yes	Neg.	S	8-3 / 3735	None	Barium sulphate—distilled water	S H	S	A	No	L 1	O	Mod-M 1/3	M	No	FT	8+ 24−
39	3	B	F	Yes	Neg.	S	7-1 / 3210	None	"	S H	M	A	Yes	L 1	O	S-M 1/3	M	No	1/6	8+ 24−
40	6	W	F	Yes	Neg.	S	8-2 / 3700	None	"	R	M	S	Yes	T 12	O	Mod-M 1/3	M	No	0	8
41	5	W	F	Yes	Neg.	BD	7-5 / 3315	None	"	S H	M	L	No	L 1	O	S-M 1/3	M	No	2/5	96+ 120−
42	2	B	F	Yes	Neg.	LF	6-1 / 2760	None	"	T P	M	A	Yes	T 11	O	S-M 1/3	R	No	VFT	8
43	7	W	F	Yes	Neg.	S	8-8 / 3850	None	"	S H	M	A	Yes	T 12	O	S-L 1/3	R	No	0	8
44	5	W	M	Yes	Neg.	LF	5-15 / 2705	One loop of cord about neck	"	S H	M	A	No	L 1	O	S-L 1/3	M	No	1/8	8+ 24−
45	3	W	M	Yes	Neg.	S	7-12 / 3530	Maternal hypertension; four misc.	"	S H	S	S	No	T 12	O	S-M 1/3	M	No	0	3
46	5	W	F	Yes	Neg.	S	6-11 / 3040	None	"	T P	S	A	No	T 12	O	S-L 1/3	M	No	0	8
47	2	B	M	Yes	Neg.	S	5-10 / 2545	None	"	S H	M	S	No	L 1	O	S-L 1/3	M	No	1/4	48+
48	2	W	F	Yes	Neg.	S	8-10 / 3915	None	"	S H	M	A	No	L 2	O	Mod-L 1/3	R	No	1/10	8+ 24−
49	3	B	F	Not recorded	Neg.	S	5-12 / 2600	None	"	R	S	S	Yes	T 12	O	S-M 1/3	M	No	FT	8+ 24−
50	7	W	M	Yes	Neg.	LF	6-12 / 3050	One loop of cord about neck	"	S H	L	A	Yes	L 1	O	S-L 1/3	S	No	0	6
51	4	W	F	Yes	Neg.	LF	7-5 / 3325	None	"	S H	M	A	No	L 2	O	S-L 1/3	S	No	0	8+ 24−
52	4	W	M	Yes	Neg.	S	6-7 / 2920	None	"	T P	L	A	No	T 12	Ho	S-L 1/3	S	No	1/10	24+ 48−
53	4	W	F	Not recorded	Neg.	S	5-12 / 2615	None	"	R	S	S	Yes	L 1	O	Mod-M 1/3	M	No	FT	8+ 24−
54	4	W	M	Yes	Neg.	BD	8-7 / 3840	None	"	Sc	M	A	No	L 1	Ho	S-M 1/3	S	No	2/5	24+ 48−
55	3	B	F	Yes	Neg.	LF	6-14 / 3115	None	"	R	M	A	No	T 11	O	Mod-L 1/3	M	No	1/4	24+ 48−

* (Delivery) S = Spontaneous; LF = Low forceps; CS = Cecarean Section; PV = Podalic version; BD = Breech delivery.
† (Shape of Stomach) FH = Fishhook; SH = Steerhorn; R = Retort; TP = Tobacco pouch; Sc = Scaphoid.
‡ (Size of gas bubble) S = Small; M = Medium; L = Large.
§ (Size of stomach) A = Average; S = Small; L = Large.
‖ Position of greater curvature in relation to vertebral level in erect position.
¶ (Tonicity) O = Orthotonic; Ho = Hypotonic; Hr = Hypertonic.
** (Peristalsis—Character and location of beginning waves) S = Shallow; Mod = Moderate; D = Deep; U = Upper; M = Middle; L = Lower
†† (Early gastric motility) S = Slow; M = Moderate; R = Rapid.

TABLE I—*Continued*

Small Intestine															Colon							
		Continuous Small Bowel Loops						Segmentation of Small Bowel														
		A = Throughout Examination B = Early, that is, during 1st 2 to 3 hr. C = Late, that is, after 1st 2 to 3 hr. 1+ = Slight 2+ = Moderate 3+ = Marked J = Jejunum I = Ileum																			
Special small intestine study	Duodenal cap visualized	A		B		C		A		B		C		Time in hours for meal to enter cecum	Location of head of meal in 8 hr.	Appendix visualized	Amount of meal evacuated from colon in 24 hours 0 = None 1+ = Trace only 2+ = Moderate amount 3+ = Marked amount 4+ = Complete						Remarks
		J	I	J	I	J	I	J	I	J	I	J	I				0	1+	2+	3+	4+		
No	Yes			1+									2+	4	Sigmoid	No					x	
Yes	Yes			2+	1+							1+	2+	3	Desc. colon	No				x		
Yes	Yes			1+					2+			1+		3	Desc. colon	No					x	
No	Yes							2+	2+					6	Transv. colon	No				x		
Yes	Yes			2+	2+							2+	2+	3	Desc. colon	No					x	
No	Yes			1+	1+								2+	3	Desc. colon	No					x	
No	Yes			1+									2+	6	Desc. colon	No	x					
Yes	Yes				3+			2+		2+			2+	4	Sigmoid	No					x	
Yes	Yes			2+	2+							1+	2+	4	Sigmoid	No				x		
Yes	Yes							3+	3+					5	Mid-desc. colon	No			x			
Yes	Yes			3+	3+							1+	2+	2	Desc. colon	No					x	Rapid early gastric motility
Yes	Yes							2+	2+					3	Desc. colon	No					x	
No	Yes	2+	2+											?	Transv. colon	No					x	
No	Yes		2+							1+				?	Asc. colon	No				x		
Yes	Yes							3+	3+					3	Evacuated 4 hr.	No				x		
Yes	Yes			2+	2+							2+	3+	3½	Rectum	No					x	Milk formula at 2½ hours
Yes	Yes							2+	2+					4½	Sigmoid	No				x		
Yes	Yes								2+			2+		4	Transv. colon	No				x		

TABLE I—*Continued*

Newborn Number	Age in days	Color	Sex	Full term	Maternal serology	*	Birth weight lb.-oz. / gm.	Complications	Stomach											
									Type of meal	†	‡	§	Cascading	‖	¶	**	††	Pyloro-spasm	Amount of meal remaining at 8 hr. T = Trace; FT = Faint trace VFT = Very faint trace	Emptying time in hours + after numeral = "more than"; − after numeral = "less than"
56	3	B	F	8½ mo.	Neg.	S	6-5 / 2870	None	Barium sulphate—distilled water	S H	S	A	No	L 1	O	S-M 1/3	R	No	0	6
57	2	B	M	Yes	Neg.	S	7-5 / 3310	None	"	S H	M	A	No	T 12	O	S-M 1/3	R	No	1/10	30+
58	5	W	F	Yes	Neg.	S	7-1 / 3200	None	"	S H	M	A	No	L 2	O	S-M 1/3	S	No	1/6	24+ 48−
59	6	W	F	Yes	Neg.	S	6-6 / 2880	None	"	S H	L	A	No	L 2	Ho	Mod-M 1/3	M	No	1/6	8+ 24−
60	4	W	M	Yes	Neg.	S	6-12 / 3050	None	"	S H	M	A	No	L 3	O	Mod-M 1/3	M	No	1/8	8+ 24−
61	5	B	M	Yes	Neg.	S	7 / 3170	None	"	S H	M	L	No	L 3	Ho	S-M 1/3	S	No	1/4	8+ 24−
62	5	W	F	Yes	Neg.	S	7-1 / 3205	None	"	T P	M	A	Yes	L 1	O	Mod-M 1/3	M	No	1/4	55+
63	6	B	F	Yes	Neg.	S	6-11 / 3030	None	"	R	M	A	No	T 12	O	S-M 1/3	R	No	1/4	24+ 48−
64	3	W	F	Yes	Neg.	S	7-4 / 3300	None	"	R	M	S	No	T 12	O	Mod-M 1/3	S	No	FT	8+ 24−
65	6	B	M	Yes	Neg.	S	7-12 / 3540	None	"	T P	M	A	Yes	T 12	O	D-U 1/3	S	1+	1/4	24+
66	5	B	M	Yes	Neg.	S	6-11 / 3044	None	"	T P	M	A	Yes	T 12	O	Mod-M 1/3	M	No	1/6	24+
67	3	B	F	Yes	Neg.	S	6-14 / 3115	None	Gum-arabic barium sulphate-distilled water	S H	M	A	No	L 1	O	S-M 1/3	M	No	2/5	24+ 48−
68	5	W	M	Yes	Neg.	LF	8-6 / 3800	None	"	T P	M	A	Yes	T 12	O	S-M 1/3	M	No	1/10	24+ 48−
69	4	W	M	Yes	Neg.	S	7-8 / 3405	None	"	R	L	S	No	T 12	Ho	S-L 1/3	R	No	T	24+ 48−
70	3	B	M	Yes	Neg.	S	7-2 / 3235	None	"	S H	S	A	Yes	L 2	O	S-L 1/3	M	No	1/10	24+ 48−
71	3	B	M	Yes	Neg.	S	7-2 / 3240	None	"	R	L	A	Yes	L 1	Ho	Mod-M 1/3	M	No	1/6	8
72	5	W	M	Yes	Neg.	LF	6-13 / 3110	None	"	R	S	A	Yes	T 11	O	S-M 1/3	R	No	0	6
73	4	W	F	Not recorded	Neg.	S	Not recorded	None	"	S H	M	A	No	L 1	O	Mod-L 1/3	M	No	1/10	24+ 48−
74	7	W	F	7½–8 mos.	Neg.	S	6-10 / 3020	None	"	T P	L	A	No	T 12	Ho	S-L 1/3	R	No	0	6

* (Delivery) S = Spontaneous; LF = Low forceps; CS = Cesarean Section; PV = Podalic version; BD = Breech delivery.
† (Shape of Stomach) FH = Fishhook; SH = Steerhorn; R = Retort; TP = Tobacco pouch; Sc = Scaphoid.
‡ (Size of gas bubble) S = Small; M = Medium; L = Large.
§ (Size of stomach) A = Average; S = Small; L = Large.
‖ Position of greater curvature in relation to vertebral level in erect position.
¶ (Tonicity) O = Orthotonic; Ho = Hypotonic; Hr = Hypertonic.
** (Peristalsis—Character and location of beginning waves) S = Shallow; Mod = Moderate; D = Deep; U = Upper; M = Middle; L = Lower.
†† (Early gastric motility) S = Slow; M = Moderate; R = Rapid.

TABLE I—*Continued*

Small Intestine															Colon							
		Continuous Small Bowel Loops						Segmentation of Small Bowel														
		A = Throughout Examination B = Early, that is, during 1st 2 to 3 hr. C = Late, that is, after 1st 2 to 3 hr. 1+ = Slight 2+ = Moderate 3+ = Marked J = Jejunum I = Ileum																			
Special small intestine study	Duodenal cap visualized	A		B		C		A		B		C		Time in hours for meal to enter cecum	Location of head of meal in 8 hr.	Appendix visualized	Amount of meal evacuated from colon in 24 hours 0 = None 1+ = Trace only 2+ = Moderate amount 3+ = Marked amount 4+ = Complete						Remarks
		J	I	J	I	J	I	J	I	J	I	J	I				0	1+	2+	3+	4+		
No	Yes			3+	3+		3+							?	Asc. colon	No	x					Rapid early gastric motility
No	Yes			2+							2+		2+	2½	Desc. colon	No					x	Milk formula at 2½ hours
No	Yes			1+									1+	?	Prox. tr. colon	No			x			
No	Yes			1+									2+	?	Sigmoid	No			x			
Yes	Yes			1+	1+								3+	5½	Sigmoid	No				x		Markedly dilated ileal loops
Yes	Yes			1+					2+			1+		6	Hepatic flexure	No				x		
Yes	Yes											2+	3+	5	Dec. colon	No	x					
No	Yes			2+	2+								2+	?	Sigmoid	No				x		Milk formula at 2½ hours
Yes	Yes			1+		1+			2+					5	Desc. colon	No				x		
No	Yes			1+					2+			1+		4	Evacuated	Yes			x			Milk formula at 2½ hours
No	Yes			1+	2+		2+					1+	1+	4	Sigmoid	No				x		Milk formula at 2½ hours
No	Yes											2+	2+	6	Desc. colon	No			x			
Yes	Yes							3+	3+					4	Sigmoid	No				x		
Yes	Yes			3+	2+							1+	2+	4	Desc. colcn	No		x				Rapid early gastric motility
Yes	Yes			3+	2+	1+	2+					1+	1+	5	Desc. colon	No				x		Rapid early gastric motility
Yes	Yes			2+	2+							1+	3+	4	Sigmoid	No					x	
No	Yes			3+										4	Sigmoid	No				x		Rapid early gastric motility
Yes	Yes							2+	3+					4	Sigmoid	No				x		
No	Yes			3+	2+								1+	4	Sigmoid	No					x	Rapid early gastric motility

TABLE I—*Continued*

Newborn Number	Age in days	Color	Sex	Full term	Maternal serology	*	Birth weight lb.-oz. / gm.	Complications	Stomach												Special small intestine study
									Type of meal	†	‡	§	Cascading	‖	¶	**	††	Pyloro-spasm	Amount of meal remaining at 8 hr. T = Trace; FT = Faint trace; VFT = Very faint trace	Emptying time in hours + after numeral = "more" than"; − after numeral = "less than"	
75	3	B	F	Yes	Neg.	S	6-9 / 3005	None	Gum arabic barium sulphate-distilled water	S H	M	A	No	L 2	O	S-M 1/3	M	No	1/8	24+ 48−	Yes
76	3	B	M	Not recorded	Neg.	S	5-15 / 2695	None	"	R	S	A	Yes	T 12	O	S-L 1/3	R	No	VFT	8	No
77	5	W	F	Yes	Neg.	S	8-8 / 3875	None	"	S H	S	A	No	L 2	O	Mod-M 1/3	R	No	0	6	No
78	4	B	M	8 mos.	Neg.	S	6 / 2710	None	Gum-arabic barium sulphate-milk formula	S H	S	S	No	L 1	O	Very S-M 1/3	S	No	1/8	24+ 48−	No
79	6	B	F	Yes	Neg.	S	6-15 / 3145	None	"	R	S	A	No	T 12	O	Mod-M 1/3	R	No	1/10	24+ 84−	No
80	7	W	M	Not recorded	Neg.	LF	6-7 / 2925	None	"	T P	S	A	Yes	T 12	O	Mod-M 1/3	M	No	T	8+ 24−	No
81	2	B	F	Not recorded	Neg.	S	7-3 / 3275	None	"	T P	S	S	No	T 12	O	Mod-L 1/3	R	No	1/2	24+	No
82	2	W	M	Yes	Neg.	S	8-14 / 4020	None	"	T P	L	S	No	T 12	O	S-L 1/3	S	No	1/2	72+ 96−	No
83	3	W	M	Yes	Neg.	LF	7-8 / 3400	None	"	T P	S	S	No	T 12	O	S-L 1/3	M	No	T	8+ 24−	No
84	5	W	F	Yes	Neg.	LF	7 / 3185	None	"	S H	M	S	No	T 12	O	S-L 1/3	R	No	0	7	No
85	7	W	F	Not recorded	Wass. 4+ Kahn 4+	S	5-13 / 2650	None	"	R	M	A	Yes	T 12	O	Mod-M 1/3	R	No	VFT	8	No
86	4	W	M	Yes	Neg.	S	7-6 / 3350	None	"	S H	S	S	Yes	T 12	O	S-L 1/3	S	No	1/10	8+ 24−	No
87	9	W	M	8½ mos.	Neg.	S	5-8 / 2500	None	"	S H	M	A	No	L 2	O	Mod-M 1/3	M	No	0	7	No
88	5	W	M	Yes	Neg.	S	8-13 / 4010	None	"	T P	S	S	Yes	T 12	O	Mod-M 1/3	M	No	T	8+ 24−	No
89	3	B	M	Yes	Wass. 2+	S	8-5 / 3790	None	"	S H	S	S	No	T 12	O	Mod-M 1/3	R	No	0	6½	No
90	3	B	F	Not recorded	Neg.	S	5-12 / 2615	None	"	S H	S	A	No	L 1	O	S-M 1/3	R	No	1/6	48+ 72−	No
91	3	B	F	Not recorded	Neg.	LF	6-14 / 3115	None	"	R	S	S	No	T 12	O	S-L 1/3	M	No	1/6	8+ 24−	No

* (Delivery) S = Spontaneous; LF = Low forceps; CS = Cesarean Section; PV = Podalic version; BD = Breech delivery.
† (Shape of Stomach) FH = Fishhook; SH = Steerhorn; R = Retort; TP = Tobacco pouch; Sc = Scaphoid.
‡ (Size of gas bubble) S = Small; M = Medium; L = Large.
§ (Size of stomach) A = Average; S = Small; L = Large.
‖ Position of greater curvature in relation to vertebral level in erect position.
¶ (Tonicity) O = Orthotonic; Ho = Hypotonic; Hr = Hypertonic.
** (Peristalsis—Character and location of beginning waves) S = Shallow; Mod = Moderate; D = Deep; U = Upper; M = Middle; L = Lower.
†† (Early gastric motility) S = Slow; M = Moderate; R = Rapid.

TABLE I—*Continued*

Small Intestine																Colon							Remarks
		Continuous Small Bowel Loops						Segmentation of Small Bowel										Amount of meal evacuated from colon in 24 hours						
Special small intestine study	Duodenal cap visualized	A = Throughout Examination B = Early, that is, during 1st 2 to 3 hr. C = Late, that is, after 1st 2 to 3 hr. 1+ = Slight 2+ = Moderate 3+ = Marked J = Jejunum I = Ileum												Time in hours for meal to enter cecum	Location of head of meal in 8 hr	Appendix visualized	0 = None 1+ = Trace only 2+ = Moderate amount 3+ = Marked amount 4+ = Complete						
		A		B		C		A		B		C						0	1+	2+	3+	4+	
		J	I	J	I	J	I	J	I	J	I	J	I										
Yes	Yes			2+	1+							1+	2+	3½	Splenic flexure	No					x		
No	Yes			1+									2+	?	Sigmoid	No					x		
No	Yes			2+	2+							1+	2+	4	Desc. colon	No						x	
No	No					1+		2+	2+					7	Transv. colon	No				x			
No	Yes			2+	2+									4+	Evacuated	No						x	
No	Yes			2+								2+	2+	6	Sigmoid	No						x	
No	Yes			2+									2+	?	Desc. colon	No	x						
No	No							2+	2+					8	Asc. colon	No			x				
No	Yes							2+	2+					?	Splenic flexure	No						x	
No	Yes							2+	2+					?	Sigmoid	No						x	
No	Yes											2+	2+	4	Sigmoid	No					x		
No	Yes						2+						1+	?	Transv. colon	No	x						
No	Yes			2+	2+		3+							?	Transv. colon	No	x						
No	Yes							2+					2+	6	Desc. colon	No					x		
No	Yes			2+	2+								2+	?	Rectum	No						x	
No	Yes			2+									2+	?	Desc. colon	No			x				
No	Yes			1+									2+	?	Desc. colon	No						x	

TABLE I—*Continued*

Newborn Number	Age in days	Color	Sex	Full term	Maternal serology	*	Birth weight lb.-oz. / gm.	Complications	Stomach												Special small intestine study
									Type of meal	†	‡	§	Cascading	‖	¶	**	††	Pyloro-spasm	Amount of meal remaining at 8 hr. T = Trace; FT = Faint trace; VFT = Very faint trace	Emptying time in hours + after numeral = "more than"; −after numeral = "less than"	
92	7	W	F	Not recorded	Neg.	S	6-13 / 3100	None	Gum-arabic barium sulphate-milk formula	TP	M	A	Yes	T 12	O	Mod-M 1/3	R	No	FT	8+ 24−	No
93	5	W	F	Yes	Neg.	S	7-5 / 3325	None	Barium meal distilled water	R	L	L	No	L 1	Ho	S-M 1/3	R	No	1/6	24+	No
94	4	B	M	Yes	Neg.	S	6-12½ / 3085	None	"	S H	M	A	No	L 1	O	S-M 1/3	S	No	1/4	24+ 48−	No
95	2	W	M	Yes	Neg.	S	8-13 / 4000	None	"	R	M	A	Yes	L 1	O	S-U 1/3	M	No	1/2	9+ 24−	No
96	4	B	M	Yes	Neg.	S	8-3 / 3735	None	"	T P	L	A	No	T 12	O	S-L 1/3	R	No	2/5	24+ 48−	No
97	3	B	M	Yes	Neg.	S	6-11 / 3035	None	"	R	L	S	No	T 11	O	S-L 1/3	S	No	1/6	8+ 24−	No
98	4	W	F	Yes	Neg.	S	8-12 / 3960	None	"	S H	S	A	No	L 4	O	S-M 1/3	S	No	1/3	168+	No
99	3	B	F	Yes	Neg.	S	6-12 / 3065	None	"	T P	M	S	No	T 11	O	S-M 1/3	S	No	1/4	8+ 24−	No
100	3	B	M	Yes	Neg.	S	5-9 / 2535	None	Barium meal-milk formula	S H	S	A	No	L 2	O	S-L 1/3	M	No	T	8+ 24−	No
101	7	B	M	Yes	Neg.	S	5-14 / 2670	None	"	S H	S	A	No	L 1	O	S-M 1/3	S	No	0	8−	No
102	5	W	F	Yes	Neg.	S	9-7 / 4275	None	"	Sc	L	A	No	L 1	Ho	Mod-L 1/3	S	No	1/10	8+ 24−	No
103	9	W	M	Yes	Kahn 4+	LF	7-12 / 3525	None	"	R	M	S	Yes	L 1	O	Mod-M 1/3	M	No	VFT	8	No
104	3	B	M	Yes	Not recorded	S	8-1 / 3665	None	"	S H	M	L	No	L 3	O	S-L 1/3	S	No	2/3	96+ 120−	No
105	7	B	F	Yes	Neg.	BD	6-2 / 2785	None	"	S H	L	L	No	L 2	Ho	S-L 1/3	S	No	0	8+	No
106	6	W	F	Yes	Not recorded	S	7-1 / 3200	None	"	F H	M	A	No	L 1	O	S-M 1/3	S	No	1/8	8+ 24−	No
107	6	W	F	Yes	Neg.	CS	7-11 / 3495	None	"	S H	L	L	No	L 2	Ho	Mod-L 1/3	M	No	T	8+ 24−	No
108	9	B	F	Yes	Neg.	LF	6-1 / 2760	None	"	S H	L	L	No	L 1	O	S-L 1/3	S	No	0	8+	No
109	7	W	F	Yes	Neg.	S	Not recorded	None	"	S H	L	L	No	L 2	O	S-M 1/3	M	No	0	6	No
110	5	B	F	Yes	Not recorded	S	8-1 / 3675	Mother has mild hypertension	"	R	M	A	No	T 12	O	S-L 1/3	S	No	1/8	24	No

* (Delivery) S = Spontaneous; LF = Low forceps; CS = Cesarean Section; PV = Podalic version; BD = Breech delivery.
† (Shape of Stomach) FH = Fishhook; SH = Steerhorn; R = Retort; TP = Tobacco pouch; Sc = Scaphoid.
‡ (Size of gas bubble) S = Small; M = Medium; L = Large.
§ (Size of stomach) A = Average; S = Small; L = Large.
‖ Position of greater curvature in relation to vertebral level in erect position.
¶ (Tonicity) O = Orthotonic; Ho = Hypotonic; Hr = Hypertonic.
** (Peristalsis—Character and location of beginning waves) S = Shallow; Mod = Moderate; D = Deep; U = Upper; M = Middle; L = Lower.
†† (Early gastric motility) S = Slow; M = Moderate; R = Rapid.

TABLE I—*Continued*

Emptying time in hours + after numeral = "more than"; −after numeral = "less than"	Small Intestine														Time in hours for meal to enter cecum	Colon								Remarks
	Special small intestine study	Duodenal cap visualized	Continuous Small Bowel Loops						Segmentation of Small Bowel							Location of head of meal in 8 hr.	Appendix visualized	Amount of meal evacuated from colon in 24 hours					
			A = Throughout Examination B = Early, that is, during 1st 2 to 3 hr. C = Late, that is, after 1st 2 to 3 hr. 1+ = Slight 2+ = Moderate 3+ = Marked J = Jejunum I = Ileum															0 = None 1+ = Trace only 2+ = Moderate amount 3+ = Marked amount 4+ = Complete					
			A		B		C		A		B		C											
			J	I	J	I	J	I	J	I	J	I	J	I				0	1+	2+	3+	4+	
8+ 24−	No	Yes			2+									2+	4	Desc. colon	No			x				
24+	No	Yes			2+	2+							2+	2+	4	Desc. colon	No		x					
24+ 48−	No	Yes			2+		1+	2+				2+		2+	4	Desc. colon	No	x						Colon dilated at 24 hours
9+ 24−	No	Yes			1+								2+	2+	4	Evacuated	No				x			
24+ 48−	No	Yes			2+								2+	2+	4	Recto-sigmoid	No			x				
8+ 24−	No	Yes											2+	2+	4	Desc. colon	No				x			Dilated duodenal loop at 8 hours
168+	No	Yes							2+	2+					5	Transv. colon	No	x						
8+ 24−	No	Yes					2+					2+		2+	?	Evacuated	No					x		
8+ 24−	No	Yes						2+			1+	1+		1+	?	Sigmoid	No				x			
8−	No	Yes						1+						1+	4	Sigmoid	No							Sent home before 24 hr. examination
8+ 24−	No	Yes												2+	4	Recto-sigmoid	No				x			
8	No	Yes									2+			2+	4	Desc. colon	No	x						
96+ 120−	No	Yes			2+							2+		1+	?	Transv. colon	No	x						Two-thirds of meal in stomach at 24 hrs.
8+	No	Yes													?	Sigmoid	No			x				
8+ 24−	No	Yes										2+		2+	4	Evacuated	No					x		
8+ 24−	No	Yes			1+							2+		2+	4	Desc. colon	No				x			
8+	No	Yes			1+							2+		2+	4	Sigmoid	No				x			
6	No	Yes				2+					2+	1+		2+	4	Sigmoid	No				x			
24	No	Yes						2+			2+		1+	1+	?	Desc. colon	No			x				

group which received feedings at four hour intervals, 43 per cent were found to have an emptying time of more than eight hours. A typical duodenal cap was visualized only once in their entire study. Usually they found the duodenum appearing as an annular structure, all portions being of approximately the same size. The jejunum in their cases was rarely visualized, while the ileum appeared as small globules of barium which might arrange themselves to show many patterns.

Ladd[14] noted a curious lack of peristalsis in the normal infant's stomach and said that the stomach appeared to squeeze out its food by contracting as a whole on its contents. The major contents of the stomach, he found, were expelled in from one and one half to two and one-half hours. Then the motility became slower, requiring four and one-half to five and one-half hours or longer for complete emptying. Ladd also found that if a new feeding without bismuth was given in three hours, this new feeding appeared to stimulate peristalsis, resulting in faster emptying time of the stomach. Bouslog and his co-workers[3] were unable to confirm this observation of Ladd.

Pisek and LeWald[18] made a study of infants varying in age from newborn of two days to twenty months. Their usual procedure was to give a bismuth subcarbonate-milk meal by gavage. The first roentgenograms were made one to five minutes later. When the infant was held in the vertical position they found that the stomach began to empty immediately after the meal had been given. Roentgenograms made thirty to forty minutes after feeding frequently revealed that one-third to one-half or more of the meal had left the stomach. Their findings agreed with those of Ladd in that after the major portion of the meal had left the stomach, motility became slower.

Carman[5] quotes Alwens and Husler who found the evacuation time for fluid food to be about three hours. Occasionally, however, they noted small bismuth residues after five hours in healthy sucklings. Using 200 cc. of pap they found the normal evacuation time was from three to three and one-half hours.

Groedel is quoted by Willox[24] to the effect that with barium sulphate the stomach empties itself twice as fast as with bismuth and that bismuth somewhat decreased the normal gastric motility.

According to Vogt[23] the time of evacuation of the stomach in the newborn amounts to one and one-half to three hours with mother's milk, but somewhat longer with cow's milk.

Willox[24] writes that Leven and Barrett observed infants from two to six months old. These infants were given 80 to 175 cc. of mother's milk or diluted cow's milk. With both types of feeding gastric emptying was found to require one and one-half to two hours. On the other hand, Rulison, according to Willox,[24] found that cow's milk mixtures seldom leave the stomach of the normal infant in less than two and one-half to three hours, and he has found milk present in the stomachs of healthy babies five hours after a feeding during hot weather.

De Backer and Van de Putte[7] examined infants all of whom were less than seven months old. They distinguished orthotonic and hypertonic stomachs, the former being most common. In the hypertonic form gastric emptying time was sometimes as short as two and one-half hours, while in orthotonic stomachs it was usually in the neighborhood of four and one-half hours. These authors also studied intestinal motility. They found that food entered the cecum in two and one-half to three hours. It had passed to the splenic flexure in five to seven hours, to the sigmoid in eight hours, and evacuation had occurred in eight to ten hours.

LeWald[15] suggests administration of the opaque meal through a catheter or stomach tube in a very young infant or an unruly older child, but says that the feeding may be given to infants from a bottle. He found that the duodenal bulb rarely shows the typical cap-like appearance in very young children.

Rogatz[19] examined a group of infants, the youngest of whom was five weeks old. He did not use any radiopaque agents but depended upon the shadows cast by the liquid and gaseous stomach contents. He found two main, constant types of stomach with fluid feedings, both being horizontal. In type 1 the shape was similar to that of a pear or flask lying on its side with a large, circular expanded fundus and a smaller narrow pyloric area. Type 2 was smooth, ellipitical or oval in shape and less common.

Rogatz[20,21] distinguishes between peristalsis and peristole. He defines peristalsis as a circular wave of contraction, appearing at regular intervals, which begins at the fundus and progresses toward the pylorus. According to this author peristolic function is seen only in the stomach and may be described as that capacity of the stomach wall to surround or grasp its contents following the ingestion of food. He found the peristolic reflex demonstrable only by the effect of very thick foods on the stomach outline. With this type of feeding the stomach was seen to contract strikingly to a small, circular or oval outline, with a very small air bubble. Following the administration of a thick vegetable gruel feeding and the occurrence of peristole, it was found that the gastric contents by peristaltic action were worked gradually toward the pyloric region. Rogatz states that habitual vomiting may be lessened or eliminated by such a change in consistency of the meal.

Hotz[11] says that the greater the volume of the meal and the lower the consistency, the greater is the size of the infant's stomach. As the consistency of the food increases, the peristaltic reaction of the stomach becomes greater. Hence, the most pronounced peristalsis is obtained with the thickest form of infant food, that is, gruel. Hotz believes that fluid nourishment inhibits peristalsis and favors air swallowing. However, according to Carman,[5] Alwens and Husler found that peristalsis was manifest in the infant stomach with both fluid and pap-like foods.

Willox[24] thinks that the foodstuff of which a meal is composed does not have in itself much, if any, effect on gastric motility, but that the more fluid a meal, the more quickly it will pass through the stomach. He found that in most cases the food passes through the pylorus intermittently and in an apparently nodular form. In his patients the average emptying time was three and three-fourths hours.

This same author found that in the prone position food tends to stay in the cardiac portion of the stomach for some time before progressing to the pyloric end and it is not seen passing into the intestine nearly so quickly as when the patient assumes the upright position. Smith and LeWald[22] demonstrate by copies of roentgenograms the value of holding the infant erect for a short time after feeding in order that it may eructate swallowed air.

Pendergrass, Ravdin, Johnston and Hodes,[17] working with adults, found that the emptying time of the stomach was prolonged when various food stuffs were added to the usual barium sulphate-water meal. They also found that the pattern and motility of the small intestine, which is ordinarily obtained in normal individuals, may, with a variation of the vehicle of the barium meal, suggest serious pathologic lesions. They believe that it is very poor practice to use water, normal saline, buttermilk, malted milk or whole milk indiscriminately as a vehicle for the barium meal. For this reason it was considered advisable to carry out the investigation of the small intestine in this present group of newborn infants by using only U.S.P. barium sulphate and distilled water.

Golden,[9] in noting some of the findings of Bouslog and his coworkers, of Dr. John Caffey and of Wetzel, states that no mucosal folds can be seen in the newborn infant's jejunum on roentgen examination; instead, they appear at some time between the first and the third or fourth month. He says that there is marked segmentation of the barium, with irregularly alternating narrow and widened areas and discontinuity of the intestinal contents. The barium

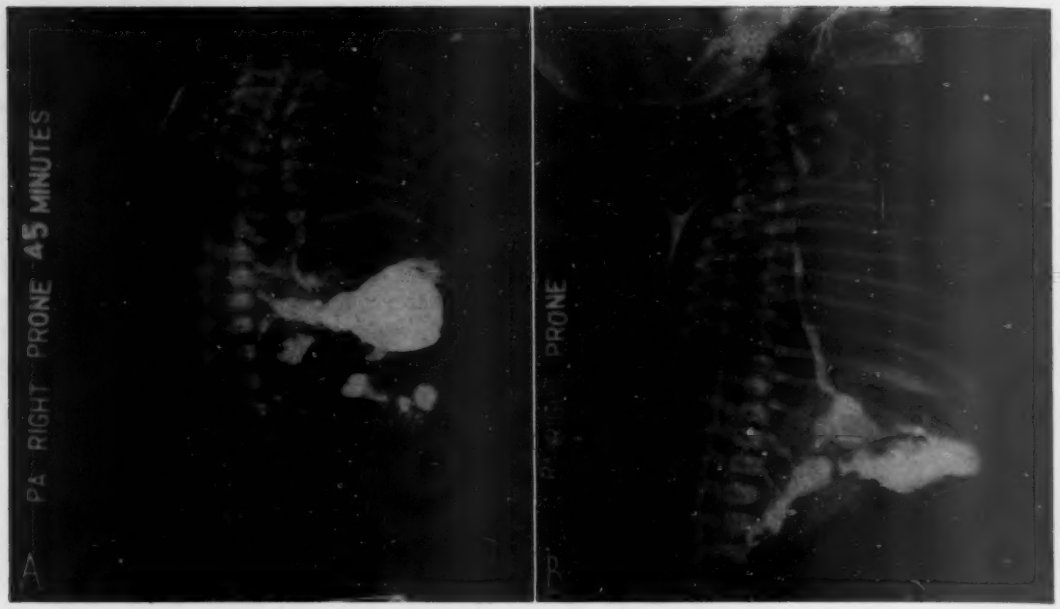

Fig. 1. *A.* (Baby H, black, aged three days.) Esophagus well outlined after administration of thin liquid barium meal. The usual degree of dilatation of the lower half of the esophagus is present.

B. (Baby N, black, aged two days.) Appearance of esophagus after giving infant a thick barium mixture.

shadow is said to become continuous some three or four months later. In several infants examined by Caffey the barium did not reach the cecum in five to six hours. Wetzel, according to Golden, found that the mucosal folds of the newborn infant's small intestine are shorter in length and height than in the adult. He also found that the mucosa of the intestine in the newborn is more developed than the muscle coat, but that the muscularis mucosae for some reason is incapable of throwing it up into folds.

Fig. 2. (Baby S, white, aged five days.) With infant recumbent after a barium meal the stomach usually appears on the roentgenogram as a round white ball in the left upper abdomen, with a gas pocket to the right and below.

FINDINGS OF THE PRESENT STUDY

The esophagus appears as a sometimes fusiform, sometimes straight tube with smooth contours (Fig. 1). The lower half nearly always distends to greater size than the upper half. Sometimes there is a considerable degree of stasis in this portion, but no cases of obstruction have been en-

countered, and nothing to indicate cardiospasm has been seen.

The Stomach. In the supine position immediately after the meal has been taken the stomach generally appears as a round opaque shadow with a large tubular gas pocket leading off to the right and below. When the infant is turned into the prone position a steerhorn shape is usually seen, while in the oblique prone position the appearance is frequently like a retort. When the infant is erect the shape of the stomach differs considerably from that of the supine and prone positions. In this paper classification of the configuration of the infant's stomach has been based entirely upon the erect appearance (see Table II). The shape varies greatly, depending upon the amount of air content. When the infant cries during feeding, large amounts of air are swallowed, and the stomach may become easily four or five times the size seen when only a 2 ounce barium meal is present. In an older infant who objected strenuously to taking the meal from a bottle, and who was fed from a spoon to the accompaniment of lusty howls, the stomach became so distended with air that it occupied the entire upper abdomen from one side of the body to the other.

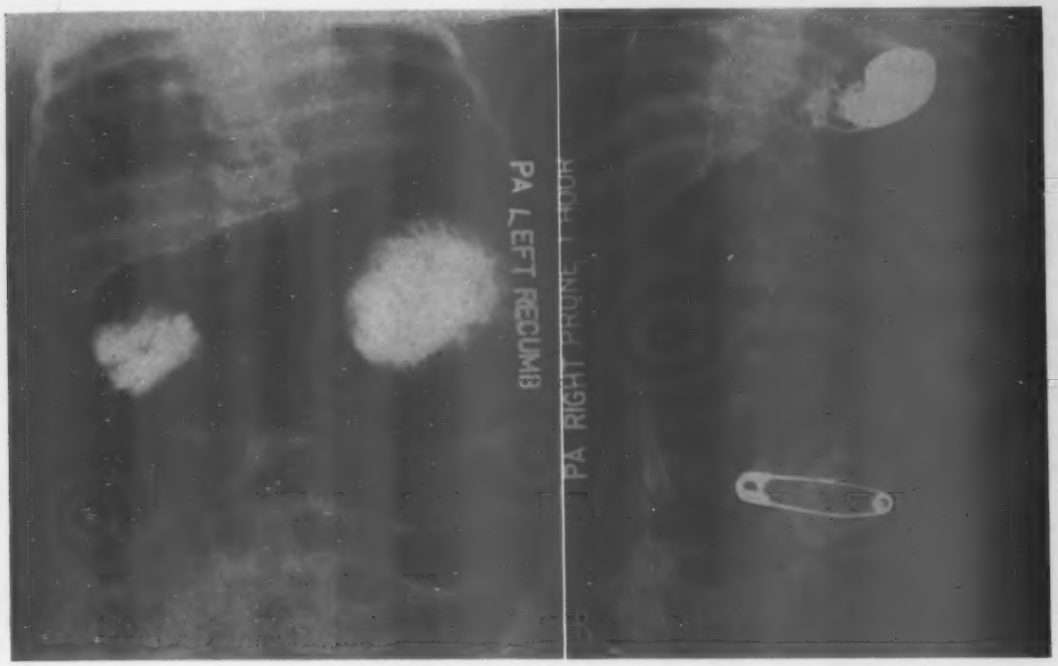

Fig. 3. *A.* (Baby S, white, aged four and one-half months.) Re-examination of same infant as Figure 2. Note extreme dilatation of stomach resulting from air swallowing on taking 1½ ounces of barium mixture from bottle, while crying vigorously.

B. The same infant one hour after taking the barium meal. The marked change in size of the stomach is due to expulsion of air. Note the amount of gas in the intestinal tract.

Table II

SHAPES OF THE STOMACH IN THE NEWBORN
(Based upon Roentgenograms with Infant Erect)

Shape	Number	Incidence of Cascading
Scaphoid	3	
Modified fish-hook	3	
Retort	20	10
Tobacco pouch	25	16
Steer-horn	59	9

Pisek and LeWald,[18] and Bouslog and associates[3] found that the infant stomach

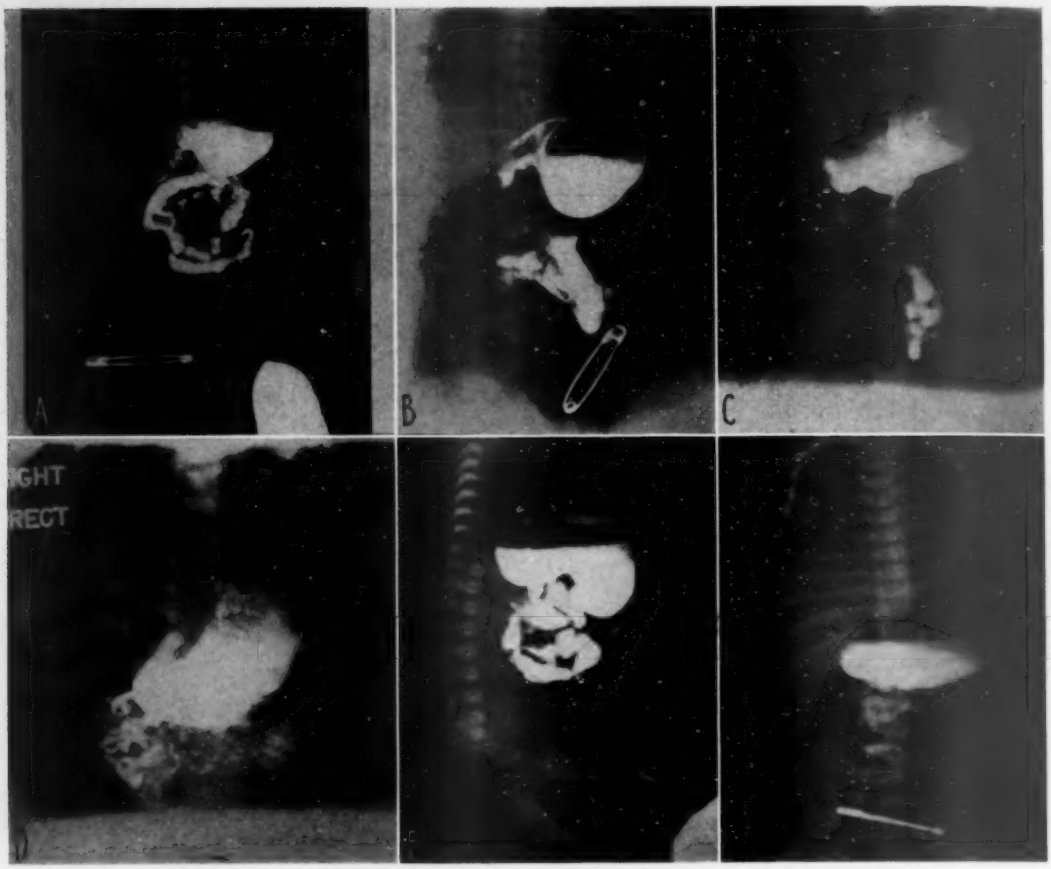

FIG. 4. Various configurations of the stomach in the newborn infant.

A. (Baby F, black, aged three days.) Tobacco pouch, a commonly seen type.

B. (Baby H, black, aged two days.) Retort, another common form.

C. (Baby W, black, aged four days.) Steer horn. This appears to be the most frequently seen type in infants. Note shallow peristaltic waves.

D. (Baby N, black.) Fish hook. This form of stomach is rare in the newborn (duodenal cap is well filled.)

E. (Baby P, black, aged three days.) Cascade or water-fall type. Cascading was noted in 35 out of 110 infants.

F. (Baby D, white, aged five days.) Scaphoid (this might equally well be called a steer horn type).

does not have a constant form. The latter group distinguished "pear," "oval," "retort" and "tobacco pouch" shapes. In many instances a true cascade type is found. As previously noted, Rogatz[19] suggested a classification of pear- or flask-like and elliptical or oval stomachs.

Peristalsis in the stomach of the newborn is very intermittent. When the infant is sleeping the stomach appears hypotonic and no peristaltic movements occur. Feeding usually stimulates contractions which may be very shallow and difficult to visualize, or the waves may be moderately deep and segmenting in type, in which case they are often seen to go through to the pylorus. Simple change of position may initiate contraction waves, and gentle massage of the abdomen over the stomach almost always results in some peristalsis. As a rule spontaneous contractions are seen only in the pyloric antrum and, less often, in the middle third, but they have been noted in the upper third.

Contraction of the newborn infant's stomach similar to that described by Rogatz[20,21] as the peristolic reflex has been frequently seen when a barium sulphate-water meal was used. This would indicate that the use of very thick foods is not necessary in eliciting this reflex. Following gentle massage of the abdomen the infant regurgitates air. A stomach which has been dilated to large size with swallowed air and barium-water mixture may now be seen to contract to but a fraction of its former size. Peristalsis is then, as Rogatz has found, much more evident.

Gastric motility is usually not commensurate with visible peristalsis. True pylorospasm is rarely seen, but at times good contractions may occur with little or no resulting evacuation of barium. At other times no definite waves are visualized, yet considerable amounts of barium are seen leaving the stomach. Motility is much more variable than in adults. During the period of taking the meal from a bottle emptying time is often rather rapid. Then a period of an hour or more may elapse in which no motility worthy of mention occurs. This may be followed by active peristalsis with evacuation of a large part of the remaining barium. Following this a period of rest often ensues and the residual meal shows only slight change in amount for several hours. On the other hand, some infants exhibit no gastric peristalsis and no motility during the feeding, nor for perhaps an hour thereafter. Yet the final emptying time may be actually shorter than in infants whose stomachs begin to empty immediately. As a rule the greatest amount of emptying takes place during the first one and one-half to two hours after the meal.

Position. As infants are observed roentgenoscopically and on roentgenograms the stomach usually appears high and close to the diaphragm. This is particularly true in the recumbent position. In the erect posture, however, the greater curvature has been seen any place from the level of the first lumbar to that of the first sacral vertebra at various times in the same infant. The most common position is opposite the twelfth thoracic or first lumbar vertebra.

Emptying Time. In the newborn the emptying time is much longer than in older infants, children and adults. In infants of three or four months it is not uncommon to find that all of the meal has been evacuated from the stomach within two to three hours. Also, in infants of twelve to fifteen days one may often find an emptying time of four or five hours, but during the first week or ten days after birth the usual thing is to find barium remaining in the stomach at the end of eight, and frequently at the end of twenty-four hours. The reason for this delay in gastric emptying in the newborn is obscure. It is possible that it is due to (1) feeble musculature of the infant (Hooker)[10] and/or (2) a mechanical factor, that is, precipitation of barium from suspension. In many newborn infants one-half to two-thirds of the meal may be evacuated within the first two or three hours; yet a considerable amount of the meal often remains at eight hours. It is hard to explain this finding without bringing in one or both of the above factors.

TABLE III

POSITION OF THE GREATER CURVATURE OF THE NEWBORN INFANT'S STOMACH IN RELATION TO VERTEBRAL LEVELS

(Infant Erect)

Vertebra	Number
$Thoracic_{11}$	8
$Thoracic_{12}$	43
$Lumbar_1$	33
$Lumbar_2$	19
$Lumbar_3$	6
$Lumbar_4$	1

In the belief that the vehicle might influence stomach emptying time various preparations have been used, but no particular difference in emptying time was noted with any of those employed.

Pursuant to the practice of Bouslog and his associates,[3] in 11 cases the feeding consisted of 10 cc. of 2 per cent gum arabic

solution, mixed with 16 grams of U.S.P. barium sulphate and added to 2 ounces of distilled water. In 15 additional cases the vehicle was changed to the usual milk formula, but otherwise the mixture was the same. One small group of 7 infants received in each case 2 ounces of a mixture of prepared barium meal, 16 grams, and distilled water. In 11 instances the feeding consisted of 2 ounces of prepared barium meal, 16 grams, and the usual milk formula. In the largest group of 66, each infant was given a 2 ounce meal composed of U.S.P. barium sulphate, grams 16, and distilled water.

TABLE IV

EMPTYING TIME OF STOMACH IN THE NEWBORN INFANT

		Type of Meal					
		Group A Prepared Barium Meal-Water	Group B Prepared Barium Meal-Milk	Group C Gum-Arabic-$BaSO_4$-Water	Group D Gum-Arabic-$BaSO_4$-Milk	Group E $BaSO_4$-Water	Total all Groups
Emptying Time (hours) 4, or under						1	1
6, or under			1	3		6	10
8, or under			4	2	4	9	19
Over 8	Less than 24	3	4		6	27	40
24	48	3	1	6	3	17	30
48	72				1	4	5
72	96				1	1	2
96	120		1			1	2
168		1					1
No. of Cases		7	11	11	15	66	110

No abnormality has been observed in the physical progress and health of these infants in whom marked delay in evacuation was encountered. As may be noted in Tables I and IV, one infant had barium remaining in the stomach at the end of seven days. It was then removed by gastric lavage. In spite of this the infant showed a normal weight gain and appeared perfectly healthy.

As noted above, Ladd[14] found that if a feeding is given after the barium meal, there is a tendency to faster emptying, a finding which Bouslog and his group[3] could not confirm. Seven infants were given the usual barium sulphate-water meal and then followed for two and one-half hours. At this time a milk formula feeding was given. In all cases complete emptying of the stomach had not occurred at the end of eight hours. In 6 infants some barium was still present at the end of twenty-four hours.

Duodenum. The duodenal bulb was visualized in 108 babies of this group. The shape is generally rounded or button like with

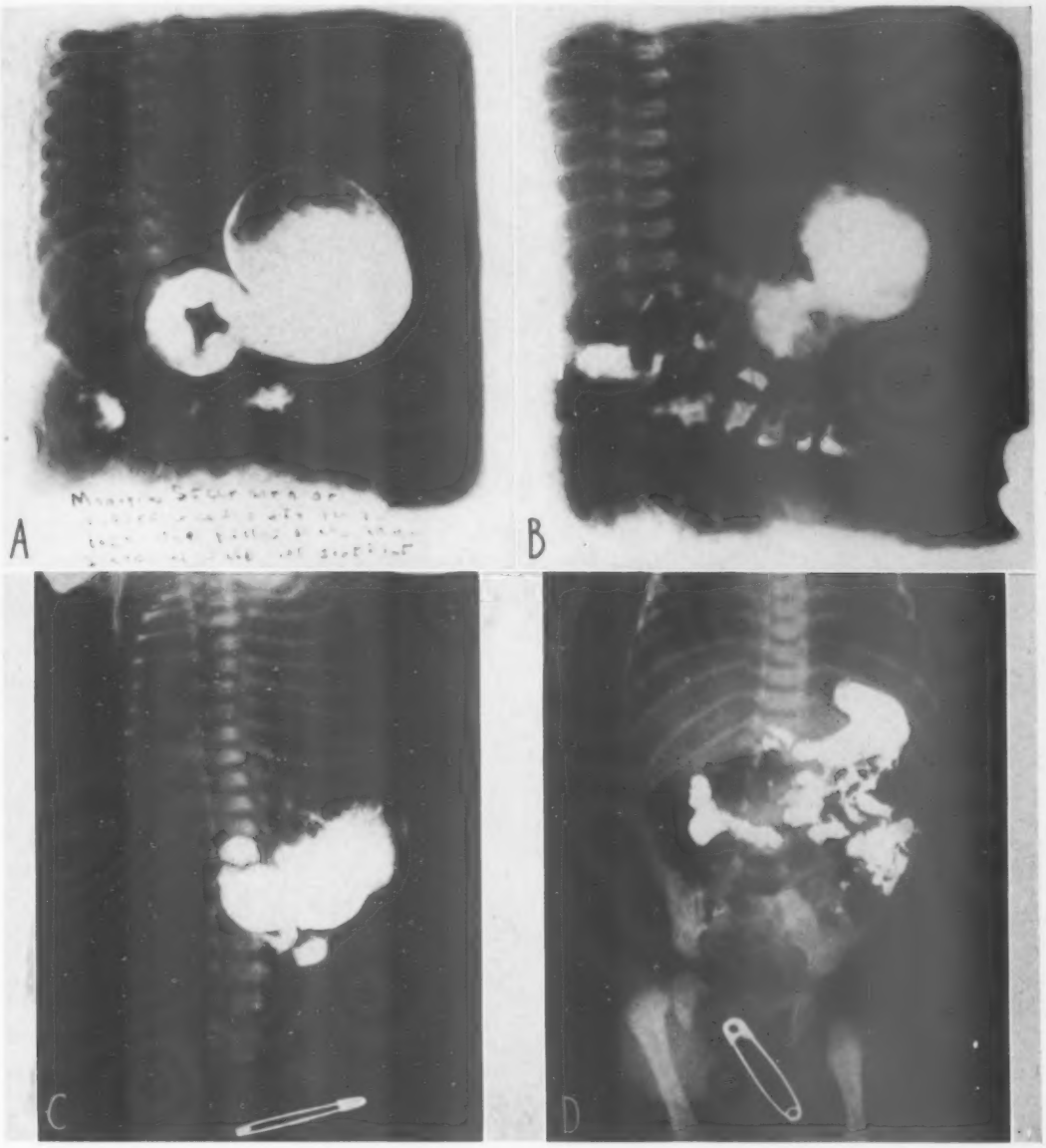

Fig. 5. Various forms of the duodenum in the newborn.

A. (Baby F, black, aged two days.) The duodenum is seen as a continuous loop, the cap not being visualized separately.

B. (Baby W, white, aged five days.) "Chocolate drop" or adult type of cap.

C. (Baby C, black, aged three days.) Round or button-like, well filled duodenal cap.

D. (Baby H, black, aged three days.) Small "chocolate drop" form of cap, visualized here four hours after infant took the meal.

smooth contours. Occasionally, a typical adult "chocolate drop" shape is seen. The cap often empties rapidly and is therefore at times difficult to visualize. Frequently, it is observed as late as four or five hours after the meal. Bouslog and his associates[3] found the duodenum appeared most often as a continuous loop with no definite demarcation of the cap. This type of filling was noted occasionally in the present study, but a distinctly outlined, rounded first portion of the duodenum has been the most

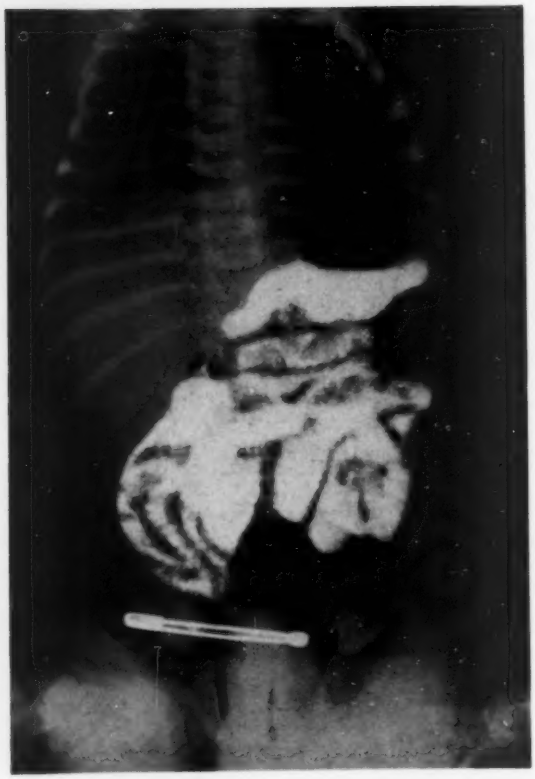

FIG. 6. (Baby S, white, aged five days.) The jejunal mucosal folds are very distinct. This appearance is uncommon in the newborn.

common observation. If the cap is retentive, it is often associated with temporary duodenal stasis. The entire duodenal loop is most readily seen by turning the infant into the right oblique prone, or even a true lateral position. It will then be noted that the pylorus and duodenum are in high position and usually directed posteriorly. If not visualized in this manner, gentle massage of the stomach to stimulate peristalsis will generally result in evacuation of enough barium to fill out the cap. Frequently, as LeWald[15] has observed, gastric emptying is more rapid when the infant is held in the erect position, and in such cases the duodenal cap can be visualized without much difficulty. The position and configuration of the remaining portion of the duodenal loop and its relationship to the stomach are the same as in adult subjects.

Jejunum and Ileum. Occasionally when gastric motility is rapid in the early part of the examination, both jejunum and ileum appear as continuous well-filled loops. When this happens, the mucosal folds of the jejunum may be well visualized. As noted previously in this paper, Wetzel found the mucosal folds of the newborn infant's small bowel to be shorter in length and height than in the adult.[9] He also found the muscularis mucosae apparently incapable of throwing the mucosal lining up into folds. That this is not always true may be seen by Figure 6.

TABLE V

STOMACH EMPTYING TIME

EFFECT OF ADDITIONAL FEEDING

(Newborn infants returned to usual milk formula 2½ hours after $BaSO_4$-water meal)

Infant Number	Amount of Barium Meal Evacuated at End of 2½ Hours	Estimated Amount of Original Barium Meal Remaining at 8 Hours	Emptying Time (hours)
1	1/3	1/5	24+
2	1/2	1/6	24+
3	4/5	Trace	8+
4	1/2	Trace	24+
5	3/5	1/4	24+
6	2/3	1/4	24+
7	1/2	1/6	24+

It is more common to find the jejunum appearing as moderately well filled, partially segmented loops, with little or no evidence of mucosal folds. Occasionally, particularly if gastric motility is slow, one may see the jejunum represented by isolated masses of barium. Later it is apt to present a continuous beaded and string-like pattern. Curiously enough, this beaded and string-like pattern is seen often as late as seven or eight hours after ingestion of the meal. Perhaps it is so visualized because of slower emptying of the stomach late in the examination, associated with greater contraction of the circular muscle of the jejunum, while in the early stages barium leaves the stomach more rapidly and the

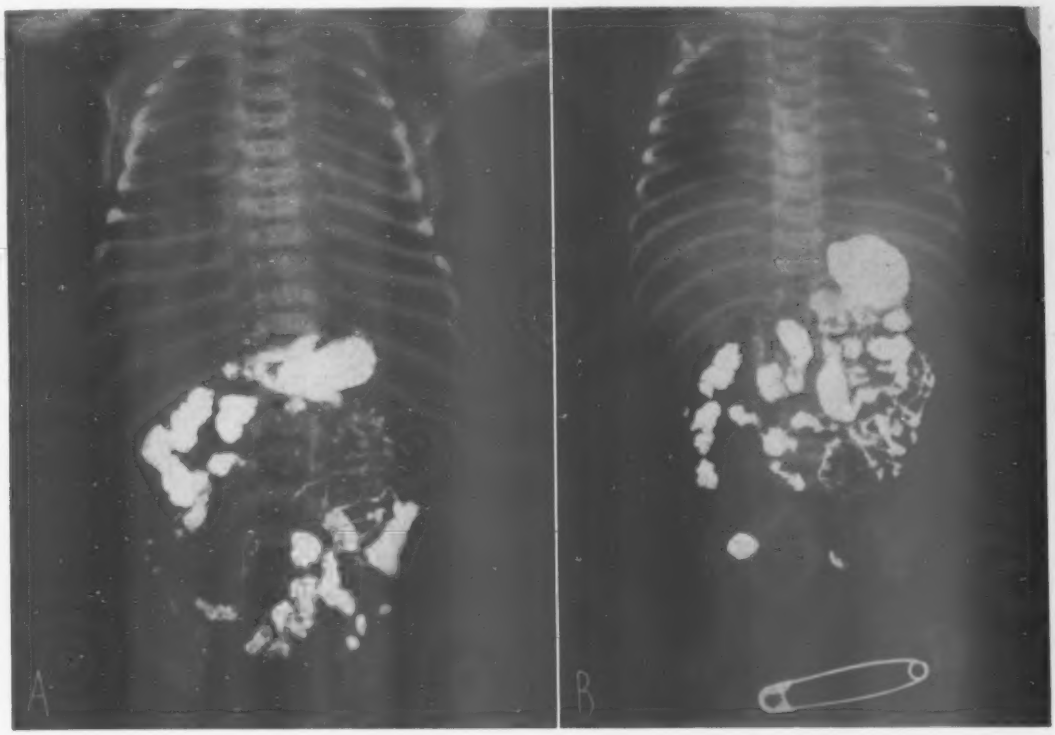

Fig. 7. *A.* (Baby K, white, aged seven days.) Examination at end of eight hours. The jejunal loops present a string-like appearance. This string-like configuration which is frequently seen in the newborn is usually found some hours after the meal, rather than early in the examination.
B. (Baby L, black, aged two days.) Examination at end of five hours. The jejunum here appears beaded. The ileum presents marked segmentation.

jejunal loops may at times be difficult to differentiate from those of the ileum.

A study of the findings in Table 1 discloses that continuity of the ileal loops during the earlier part of the examination, while frequently seen, is much less common than in the case of the jejunum. Usually after the first two or three hours the ileum is visualized as isolated segments, or, as noted by Golden,[9] as alternating narrow and widened areas, and this segmentation appears to become more marked as the examination is continued. Rarely one observes multiple long continuous ileal loops five hours or more after the meal (see Fig. 8). At other times the barium collects in one or two long straight unsegmented tubes of bowel. Sometimes the meal collects in several large masses, apparently due to marked dilatation of sections of ileum.

King and Arnold[13] say that it is a generally accepted fact that the motor activities of the small intestine depend primarily upon a local intrinsic mechanism. They also state that this has been shown in particular with reference to work on the outer longitudinal and circular musculature, but the various types of movement of the outer musculature may be modified either in the direction of augmentation or inhibition by impulse from the central nervous system via the vagi and splanchnics. They found that stimulation of the peripheral ends of the splanchnics resulted in a vigorous reaction on the part of the whole mucosa, group contraction of the villi and ridging and pitting of the mucosa. This reaction of the intestinal mucosa to splanchnic stimulation was sharpest in the duodenum, good in the jejunum and almost negative in the ileum. It is suggested by King and Arnold that the

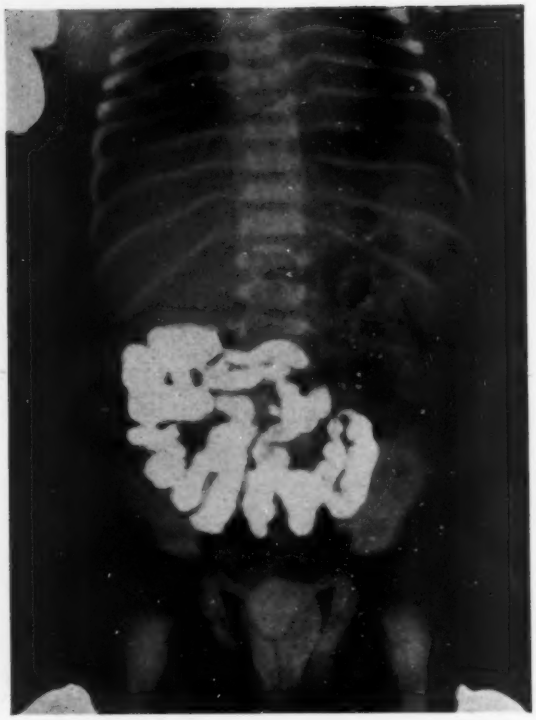

FIG. 8. (Baby P, white, aged nine days.) Examination at end of seven hours. There is unusual continuity of ileal loops. Ordinarily segmentation is marked by this time. (Stomach is empty and head of meal is in transverse colon.)

metabolic gradient of Alvarez may be the basis for a possible explanation of this finding. (This may explain in part the greater continuity of the upper small intestine in the newborn, as opposed to the segmented lower portion.)

Crandall, Chesley, Hansen and Dunbar[6] observed marked intestinal hypermotility in many patients with functional digestive tract disorders. Most of these patients had a vitamin B deficiency. As a result of the dietary deficiency, "puddling" (or segmentation) has been noted in the small bowel patterns. Golden[9] believes that the motor phenomena of the normal newborn infant's small intestine are analogous to the intestinal disturbances associated in adults with well advanced deficiency states, and that this similarity may be attributed to undeveloped nervous control in the normal infant's small intestine. This may certainly be the explanation of the findings in the newborn. However, in view of the fact that infants with rapid gastric and small bowel motility tend to show more continuity in the small intestine than in cases where the motility is slower, the analogy between the segmentation of the small intestine in dietary deficiencies and that of the normal newborn is not complete. It seems reasonable to suppose that this lack of continuity in the small bowel pattern may at times be due to the fact that the stomach usually empties intermittently in the newborn; consequently, in all likelihood only small portions of barium reach a given segment of the intestine at any one time. This is partly borne out by the fact that small particles of barium may be seen in the colon at a time when but little of the meal has left the stomach, and only small isolated collections of barium are seen in the small intestine. On the other hand, intermittent emptying of the infant's stomach does not explain the fact that the small intestine often appears early as continuous loops, while segmentation phenomena appear later.

From the observations made on the group of 50 infants in whom a special small bowel study was made, it is concluded that one may experience marked difficulty in determining whether the head of the meal is still in the ileum or whether it is in the colon. The caliber of the ileum and of the colon with an opaque meal is apt to be so nearly the same, that this alone gives no clue to the location of the barium. In one infant a single well filled loop of supposed ileum was seen in the right side of the abdomen at the end of four hours. However, the abdomen was massaged gently and the barium was discovered actually to be in the ascending colon. It was observed to pass from the ascending to the transverse and then into the descending colon, all within the space of one or two minutes. Careful roentgenoscopic and film study sometimes leaves one in doubt as to the location of the barium and in many cases it is only when the barium is seen in the rectosigmoid colon that the examiner is certain that he

has been observing barium-filled segments of colon and not ileum. There is some variation in small bowel motility, but generally barium enters the cecum in three to six hours after the meal.

TABLE VI

SMALL INTESTINAL MOTILITY

Time Required for a Barium Sulphate-Water Meal to Enter the Cecum in Newborn Infants

Number of Infants	Hours to Enter Cecum
3	2
1	2½
11	3
4	3½
16	4
1	4½
8	5
3	5½
3	6

Because of segmentation in the lower ileal loops only small amounts of barium are usually present in the ileocecal area at any one time. Consequently, it is difficult to outline the terminal ileum. In the occasional case in which it was definitely visualized this part of the small intestine appeared dilated considerably more than is ordinarily seen in adults. The cecum was never filled out to the size and smooth contour which, through barium enema studies, has been found to be the normal. In many cases a large collection of barium is present in the ileocecal area and in the ascending colon, but the cecum is not clearly demarcated. On barium enema studies it is frequently found to be similar in shape to the adult cecum, although naturally smaller. In addition, on barium enema study, it is often seen separated by a valve-like constriction from the ascending colon. This appearance has not been observed on examination by barium meal.

It is commonly known that in adults the vermiform appendix is frequently best visualized by an opaque meal. In newborn infants this is not found to be true. The appendix has been recognized only once in this group of 110 (Fig. 9). Aside from this single case, the youngest individual in whom the appendix has been demonstrated roentgenologically by a mouth meal was a four month old child at the twenty-four hour follow-up examination. On the other hand, the appendix has been seen on a number of occasions in newborn infants on barium enema study.

FIG. 9. (Baby B, black, aged six days.) The appendix is visualized on this film made at the end of six hours. This was the only infant in the group of 110 in whom the appendix was seen.

Segmentation in the colon appears to be just as common as in the ileum. The meal rarely fills parts of the colon continuously as is so often seen in adults. Instead, small segments are visualized here and there and it is usually only at the end of seven or eight hours after the meal that one sees at times a continuously filled portion of colon. This continuously filled section is usually in the descending and sigmoid area. Segmentation is another factor which makes it so difficult to be certain whether the barium is in the ileum or colon.

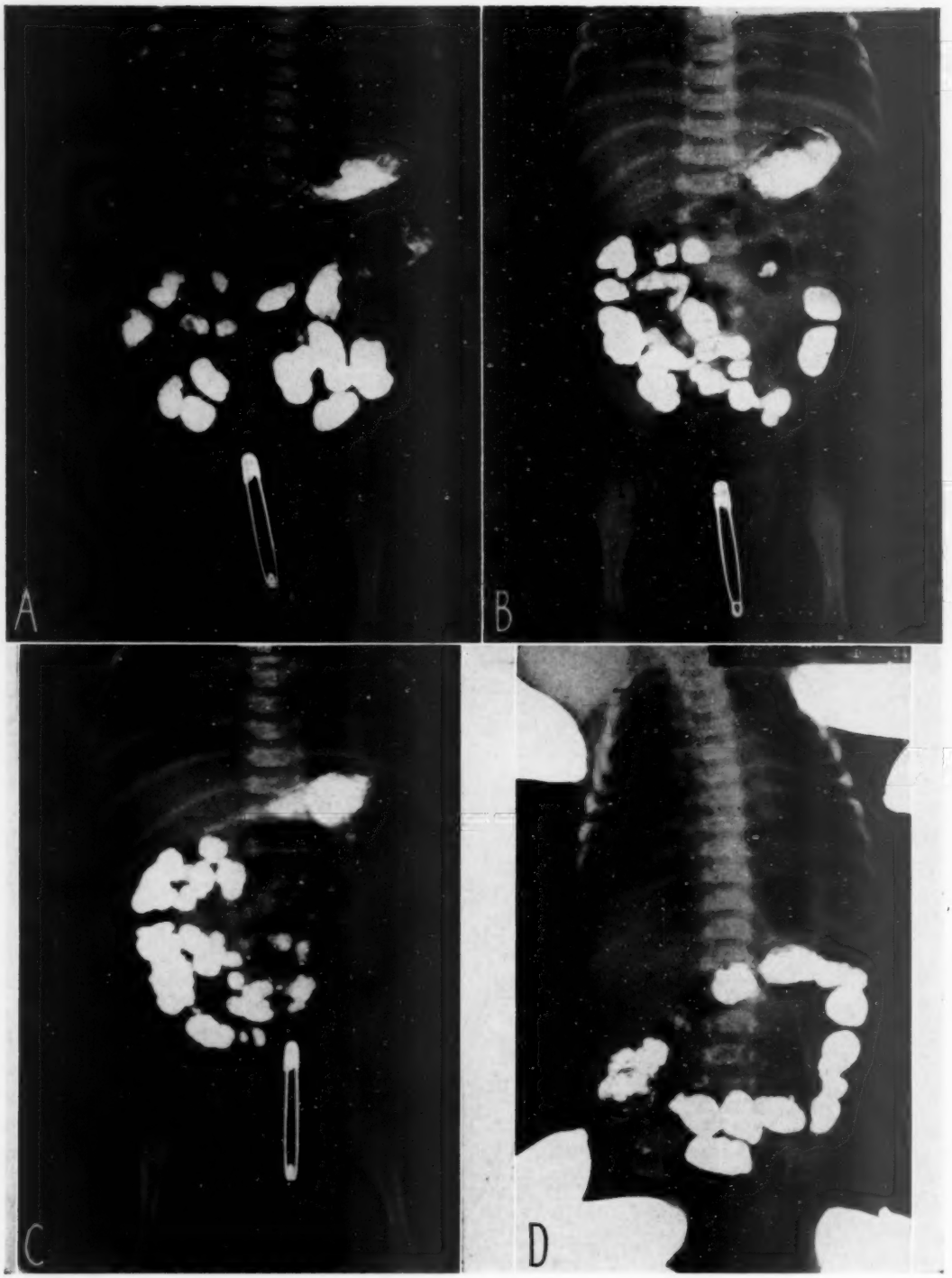

FIG. 10. *A.* (Baby W, white, aged four days.) It is often difficult to determine whether the opaque meal is in the ileum or the colon. Sections of ileum may dilate to the size of the colon and the latter is frequently segmented. Barium visualized here at five and one-half hours in left side of abdomen could be in either ileum or colon.

B. (Baby W.) Same as preceding infant—six and one-half hours. Again one cannot be certain of exact location of head of meal.

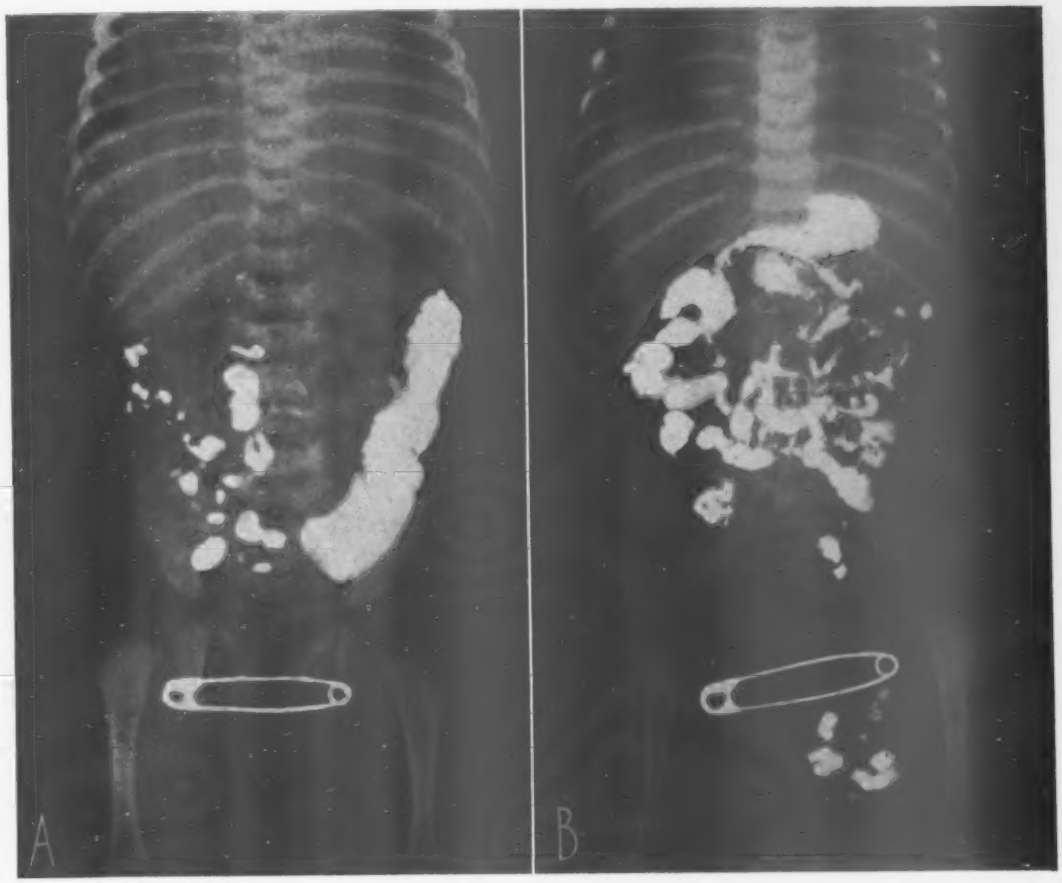

FIG. 11. *A.* (Baby P, black, aged nine days.) In the majority of infants barium is in the descending colon or sigmoid eight hours after the meal. In this case the stomach is empty, and most of the meal is in the descending colon.

B. (Baby L, black, aged two days.) In 9 of the 110 infants some of the meal had been evacuated at the end of eight hours. Here the presence of barium is noted in the baby's diaper.

Motility in the colon is in general more rapid in the infant than in the adult. Because of the difficulty in following the course of the barium in the colon no exact figures can be given. However, as noted in Table VI, barium usually enters the cecum at the end of three or four hours, rarely later than six hours. In most of the cases observed, the meal has arrived at the hepatic flexure one or two hours after entering the cecum. Passage from the hepatic flexure is relatively rapid, the head of the column generally being observed in the descending colon or sigmoid at the end of eight hours, and occasionally one sees that the meal has left the intestinal tract in eight hours.

No studies have been made on these infants between the eight hour and twenty-four hour periods. At the end of twenty-four hours most of the meal has left the intestinal tract. In an occasional infant the entire meal is collected in the colon, which

C. (Baby W.) Same as preceding infant—eight hours. It is now seen that the dilated loops in the left side of the abdomen were evidently ileum; most of meal has entered colon.

D. (Baby S, white, aged five days.) Segmented colon at six and one-quarter hours, the size and configuration of individual segments closely resembling ileum of Baby W.

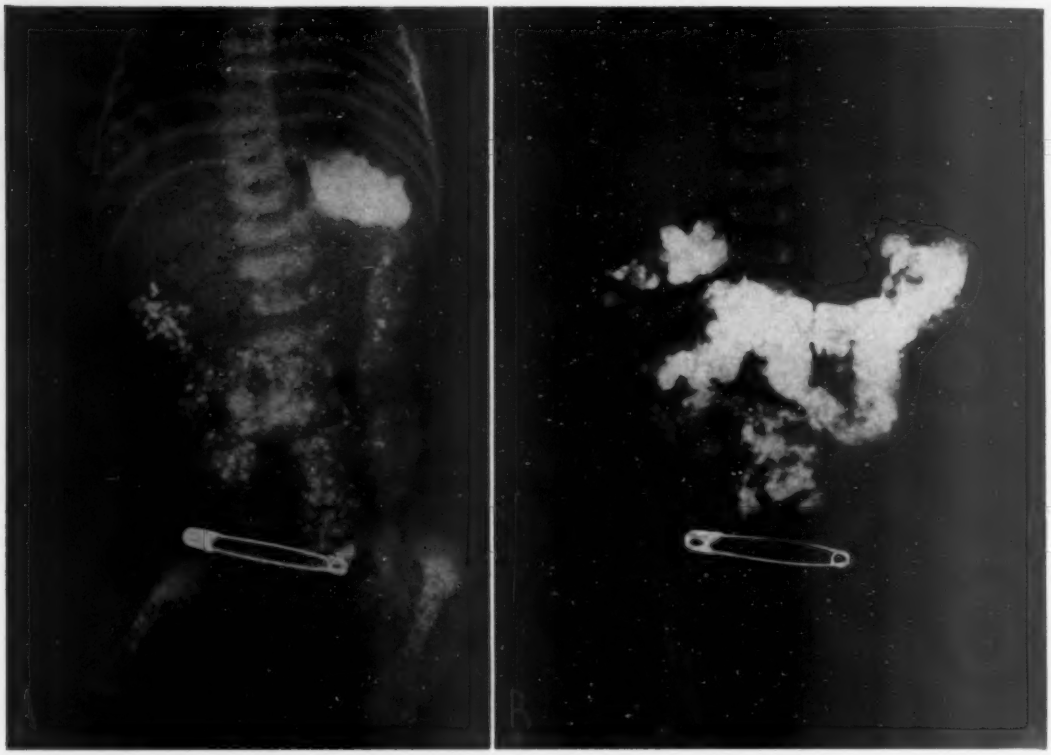

FIG. 12. The colon at the twenty-four hour examination.

A. (Baby S, black, aged four days.) A small amount of the meal remains in the stomach. Multiple barium particles are scattered throughout the colon.

B. (Baby K, white, aged seven days.) The colon in this infant is unusually well filled. Ninety-six out of 108 infants seen at the twenty-four hour period had evacuated at least part of the meal.

appears continuously dilated from cecum to rectum, but this is unusual. The common observation is to find only small masses or particles of barium here and there, while the remainder has been evacuated.

TABLE VII

INTESTINAL MOTILITY

Position of Head of Barium Meal at 8 Hours	
Location	Number of Infants
Cecum	3
Hepatic flexure	3
Transverse colon	16
Splenic flexure	4
Descending colon	33
Sigmoid	36
Rectum	6
Evacuated	9

An effort has been made to follow some of these infants by re-examinations, either immediately before discharge from the hos-

TABLE VIII

INTESTINAL MOTILITY

Evacuation of Barium Meal in 24 Hours	
Amount Evacuated	Number of Infants
None	12
Trace	7
Moderate (Approximately half)	13
Marked (Only traces of barium remaining in colon)	48
Complete	28
Total	108*

* Two infants not examined at 24 hours.

pital or some three or four months later. To date not enough have been re-examined to allow the presentation of any statistics. It has been noted in several cases, however, that the infant who prior to the end of the first week of life had an emptying time of eight to twenty-four hours or longer, at the age of two weeks might show complete emptying of the stomach in four to six hours. In older infants of approximately three months the emptying time has been found to be in the neighborhood of three to four hours. Some follow-up work has been done on the small intestinal tract in these older infants. In the small group so far examined the discontinuity of the small intestinal pattern seems on the whole to be as marked as in the newborn. Motility in the jejunum and ileum compares favorably with that seen during the first week of life, barium usually reaching the cecum in three to five hours. Due to difficulty in getting the mothers to return with the infants, study of colonic motility has so far not been possible in this older group.

SUMMARY

Roentgen studies were made on a group of 110 healthy newborn infants. Complete gastrointestinal tract examinations with an opaque meal were conducted on the entire group and 50 of these infants had, in addition, a detailed investigation of the small intestine.

A brief review of the embryology of the gastrointestinal tract is presented, followed by some of the established facts concerning the physiology of the fetal digestive tract.

A partial survey of literature on the roentgenology of the gastrointestinal tract in infants has been made. Most of the papers which have been previously presented appear to deal with older infants and young children, rather than strictly with the newborn.

In this study particular attention was paid to the roentgen anatomy and mechanics of the gastrointestinal tract.

Stomach. Using an arbitrary classification it was found that the most common shapes of the stomach with the infant erect were retort, tobacco pouch and steer horn. Cascading was frequently encountered. In the majority of cases the greater curvature with the infant erect was found to be in high position, at the level of the thoracolumbar junction. Size was variable, depending largely upon the amount of air which had been swallowed. While the stomach occasionally appears hypotonic, in most newborn infants it is of orthotonic type. Peristalsis was readily observed in nearly all cases, but the waves were usually quite shallow and intermittent. Occasionally deep segmenting waves were noted. True pylorospasm was not often encountered. Motility was not always commensurate with peristalsis. The most rapid emptying usually occurred during the first one and one-half to two hours after feeding. The stomach was completely empty of barium at the end of eight hours in only 30 out of 110 infants. Thirty infants had some barium remaining at the end of twenty-four hours. Changing the vehicle appeared to have no effect on gastric emptying time. Returning the infant to its usual formula two and one-half hours after taking the barium meal also made no difference in time of evacuation. If anything, it tended to prolong the emptying time of the stomach.

Duodenum. The cap which generally appeared rounded or button-like was visualized in 108 infants. Infrequently the cap was of adult "chocolate drop" shape. Rapid duodenal emptying was the rule.

Jejunum and Ileum. Occasionally when gastric motility was rapid, both jejunum and ileum appeared as continuous, well filled loops. Jejunal mucosal folds were observed occasionally, but much less commonly than in adults. Frequently the jejunum presented a beaded and string-like form. Jejunal segmentation was often noted early in the examination and it was the usual finding after the first three to four hours. The ileal appearance during the first two or three hours after ingestion of

the meal may be one of well filled, continuous loops. This is noted particularly in the upper portion. Later the ileum becomes segmented and segmentation usually increases as the examination progresses. The head of the meal reaches the cecum in three to six hours after the meal has been taken.

Ileocecal Area. The terminal ileum was not often satisfactorily visualized, due to segmentation of the distal small intestine. The appendix was visualized in only one infant out of 110 examined by opaque meal. Barium entered the cecum in three to six hours after feeding, but its usual shape was never shown satisfactorily due to small amount of barium content at any one time.

Colon. In 69 infants the meal had arrived in the lower descending colon and/or sigmoid at the end of eight hours. The head of the meal had passed only as far as the cecum in but 3 infants at this time, while in 9 some barium had been evacuated. Segmentation of the colon was as pronounced as in the small intestine and this adds greatly to the difficulty in distinguishing small from large bowel. In twenty-four hours at least a part of the meal had left the intestinal tract in 96 cases, and in 76 of these evacuation was almost or entirely complete.

I wish to express my thanks for invaluable help in this work to Dr. E. S. Carey, Resident in Radiology, and to the technicians in the Department of Radiology of the Elizabeth Steel Magee Hospital.

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DISCUSSION

Dr. Walter W. Wasson, Denver, Colo. In discussing this very fundamental paper of Dr. Henderson's, I wish to make some general remarks in regard to the gastrointestinal tract. In the first place, as physicians and radiologists, we have been in the past chiefly concerned about methods for the diagnosis of acute lesions of the gastrointestinal tract, those catastrophies which we are forced to diagnose in our daily practice. When the roentgenologist diagnoses a gallbladder disease and the surgeon removes a gallbladder that is diseased, he has removed the end-results. We have not contributed by such procedures anything to the diagnosis of the beginning of gallbladder disease. The same can be said of many of the other acute lesions of the gastrointestinal tract.

The chronic diseases of the gastrointestinal tract are much more difficult to understand than the acute ones. It is difficult for any one roentgenologist to see the gastrointestinal tract of an infant and of an adult in the same person over a period of years. Therefore, it is difficult for us to visualize the course of disease of the gastrointestinal tract. In other words, we only see the case at one time in most instances.

It is also not quite so interesting to treat the chronic diseases of the gastrointestinal tract, and then, too, there is the problem of remuneration which has handicapped treatment. However, it seems to me that we can begin to see evidence that with the development of our diagnostic procedures, we may turn to a really fundamental study of the gastrointestinal tract. This is evidenced by the recent studies of physiology of the small intestine by Dr. Golden and Dr. Pendergrass, and this paper today by Dr. Henderson is another step in that direction.

Dr. Henderson, by his exhaustive studies, has given us something very much worth while in the study of the gastrointestinal tract of the infant.

I wish to point out that the roentgen examination is the one means by which we may study the anatomy of the living, and its physiological and pathological changes through life. If Dr. Henderson will have the opportunity to follow these same infants from this age period on through life, then ten years or twenty years, or thirty years from now, he may be able to give us something as to the beginnings of some of our chronic diseases.

Dr. Robert A. Lyon, Cincinnati, Ohio. Dr. Henderson's study is of great interest to the pediatrician because it adds to our knowledge of the normal physiology and anatomy of the intestinal tract of newborn infants. Of special interest are the observations of the effects of swallowed air and the influence of sleep and the position of the infant upon the emptying time of the stomach. Information of this kind may lead us to modify feeding schedules and practices.

We are confronted by numerous abnormalities of the gastrointestinal tract of the newborn which roentgenography may help to diagnose. Congenital malformations and strictures are the most common lesions but infections and even ulcerations are not unknown. We must have a thorough knowledge of the normal appearance of the intestinal tract and the possibilities of variations in the normal infant.

Dr. Henderson has emphasized the fact that the intestinal tract of these newborn infants frequently presents patterns and positions of considerable variability which would be considered pathologic in older children and adults but are within the range of normal in the newborn.

Dr. Henderson (closing). In regard to Dr. Wasson's suggestion concerning a follow-up study on these infants through later years, I feel also that this will be a worth while procedure.

As I intimated in the paper, some follow-up studies have been made on this same group of infants, two weeks after birth, and in those cases it was found that the emptying time of the stomach was apparently more rapid than immediately after birth; also in the infants which have been re-examined at the age of three to four months, the emptying time in most cases was found to be about three hours; however, the group so far examined is too small to permit the formation of any conclusions.

LEIOMYOSARCOMA OF THE ESOPHAGUS*

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THIS case of leiomyosarcoma of the esophagus is presented to the literature because of the rarity of the lesion. Five such tumors have been previously reported. The first, described by Howard[6] in 1902 was that of a diffuse, infiltrating mass in the distal esophagus with ulcerations and metastases to the stomach and regional lymph nodes. It was a mixed cell sarcoma. The second report of leiomyosarcoma of the esophagus was made by von Hacker[5] in 1908. This was a polypoid mass filling a widely dilated lower end of the esophagus, and was a spindle cell sarcoma with no metastases. The third case, described by Mallory[7] in 1935, involved the distal third of the esophagus with extension into and ulceration of the mediastinal lymph nodes. The tumor had spread through the esophageal wall to the nodes behind the pericardium, which then enlarged to a round mass 6–7 cm. in diameter. Most of the mass was external to the esophagus.

In 1937, Menne and Birge[8] reported the only case of leiomyosarcoma involving the upper third of the esophagus on record. The tumor in this case produced a mass in the neck beginning just below the larynx and extending beneath the sternum. It was a spindle cell sarcoma. Recently, in 1941, French and Garland[4] reported the fifth known case of smooth muscle sarcoma. The tumor involved the distal third of the esophagus and was a sausage-shaped, pedunculated mass attached to the posterior esophageal wall by a narrow pedicle. The base of the tumor was continuous with the muscularis mucosae, and on microscopic section was found composed of various shaped cells. There was no extension of the growth into the adjoining regions or evidence of metastases.

REPORT OF CASE

E. H., white male, aged fifty-three, presented himself for admission February 28, 1941, to the Veterans Administration Facility, Wadsworth, Kansas, complaining of slight weakness, anorexia, occasional coughing spells, and sensation of pressure in the lower anterior chest. His family history is irrelevant. He states that he worked as a soft coal miner until eight years ago. Had malaria at the age of thirteen, aside from which he has always been well. During September, 1940, he noticed undue fatigue, impaired appetite, drowsiness, and slight cough with expectoration of mucus but no hemoptysis. States that he experienced slight dysphagia on eating meat and bread which was only present for five days and then disappeared. After two weeks' rest at home his general condition improved sufficiently to permit a return to his work for a short time as a blacksmith's helper. When admitted to the hospital, he stated that he had lost 14 pounds in weight, was troubled by persistent insomnia, and had a sensation of pressure over the lower anterior chest which made him feel that if he could only eructate gas this pressure would be relieved. On careful questioning he admitted to existing dysphagia. The insomnia was his chief complaint.

Physical Examination. Patient showed a sallow complexion and looked ill. His temperature was 99° F., pulse 90, and repiration 24. There was dullness on percussion of the chest in the region of the second and third interspaces for a distance of 1 inch to the right of the sternum. A soft systolic murmur was heard at the apex, and there was a loculated hydrocele of the right testicle. No other abnormalities were found.

Laboratory Findings. Urine, Wassermann and Kahn tests were negative. Blood count: hemoglobin, 76 per cent (11.7 gm.); erythrocytes, 5,310,000; leukocytes, 25,000; normal differential count. Gastric analysis (test without histamine): total acidity 14, no free acid, combined HCl 6, blood 4 plus, mucus 4 plus.

Roentgen Examination. Examination of the chest shows a fairly homogeneous, well defined

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Fig. 2. Left oblique view of the chest showing the spherical tumor in the posterior mediastinum.

density extending laterally from the mediastinum into the right lung field for a distance of 4 cm. (Fig. 1). This area of increased density merges with the right border of the ascending aorta for a distance of 9 cm. There is slight displacement of the lower portion of the trachea to the right. On roentgenoscopic examination

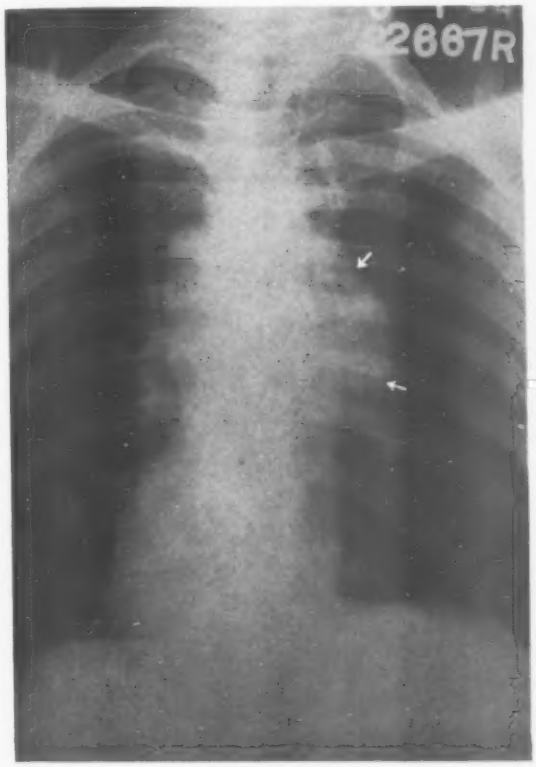

Fig. 1. Roentgenogram of the chest showing the mediastinal tumor mass originating from a leiomycsarcoma of the esophagus.

this mass was found to be spherical in outline, and located in the posterior mediastinum behind the ascending aorta, occluding the aortic window as visualized in the left oblique view (Fig. 2). There was no expansile pulsation, and the mass did not appear to be associated with the aorta. On ingestion of a barium mixture a sharp curve to the right was noted in the middle

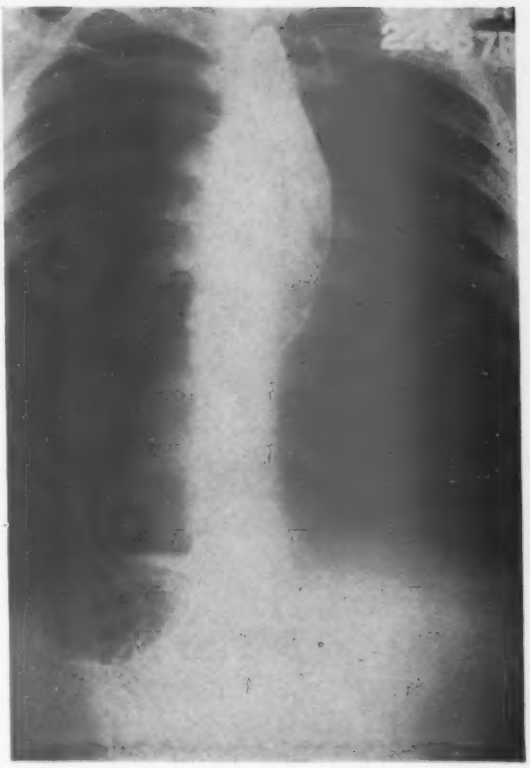

Fig. 3. Esophagus outlined with barium suspension sharply curved to the right.

Fig. 4. Filling defects in the esophagus adjoining the tumor mass in the right oblique view.

third of the esophagus in the region of the mass (Fig. 3), and an extensive filling defect was noted involving the middle third and upper part of the lower third of the esophagus (Fig. 4). The esophageal walls were irregular in outline and presented a moth-eaten appearance. A diagnosis of malignant tumor of the esophagus with secondary invasion of the mediastinum, simulating a mediastinal tumor was made.

Gastrointestinal and oral cholecystographic studies were negative. Roentgenograms of the humeri, femora, dorsal and lumbar spine, sacrum and pelvis, revealed no evidence of metastases.

Esophagoscopy and Biopsy. The patient was transferred to Hines, Illinois, tumor center for the Veterans Administration, where an esophagoscopy was performed and the following reported: At 27 cm. from the teeth a large, round, cauliflower-like mass is seen extending and protruding especially from the posterior esophageal wall. This mass produces almost complete obstruction of the lumen and bleeds readily. A biopsy was taken at that time (Fig. 5), and the pathological specimen on examination revealed the following: "Microsection reveals the wall of the esophagus in which there is spindle cell new growth in the submucosa. The new growth is highly cellular, made up of small dark hyperchromatic spindle cells closely placed; very little intercellular substance. The nuclei in the cells are quite elongated, rather thin, and the ends are quite pointed. These cells in other areas grow in interlacing bundles and are quite characteristic of smooth muscle origin. There are no mitotic figures noted. However, the cellularity and character of the cells is characteristic of malignant change. Diagnosis: leiomyosarcoma" (McNamara).

This case was seen by Dr. Max Cutler, consultant in tumors, and the following opinion expressed: "Roentgenologically, this is a lesion of approximately the middle and lower thirds

Fig. 5. Photomicrograph (approximately ×300) showing the wall of the esophagus in which there is spindle cell new growth in the submucosa of smooth muscle origin.

of the esophagus. Roentgenologically and histologically, we must consider this as a malignant tumor, which probably arose in the smooth muscle of the esophagus. The mediastinal mass could be either direct infiltration and extension of disease to surrounding tissues or possibly metastasis to the mediastinal nodes."

A gastrostomy was done under local anesthesia on April 17, 1941, because of increasing dysphagia. No abdominal masses or glands were found at operation. Patient was given deep roentgen therapy (200 kv.) over anterior and posterior fields, totalling 7,250 r. Patient was discharged from the hospital on July 3, 1941, with slight improvement.

DISCUSSION

Ewing[3] states that sarcoma of the esophagus is a rare condition occurring mostly in males ranging from four to seventy years, and is rapidly fatal. It appears either as an ulcerative process or polypoid growth. The former contains round or polyhedral cells, which metastasize early and are wide spread. The latter contains spindle cells which are free from metastases. This case and the other leiomyosarcomas previously recorded as mentioned above, conform in behavior to a great extent to these observations. Of the two possibilities as to the origin of the mediastinal mass mentioned in the report of Cutler on this case, the former is the more likely. This tumor being composed of spindle cells usually does not metastasize. Also, only the mediastinal tissues adjoining the lesion were involved and the tumor assumed a globular form very similar to the case reported by Mallory, as previously noted, which was shown at autopsy to be a direct extension from the esophagus.

The absence or the minimal degree of dysphagia in some of these cases is striking. This is possible only by reason of the fact that the tumor is frequently largely extraluminal. The patient in this case, despite the size of the mediastinal mass and the extent of esophageal involvement, when first seen made no reference to any existing dysphagia. It was only on careful questioning that he admitted some previous difficulty in swallowing several months prior to admission to the hospital, which lasted only for five days. Sante[9] speaks of a rare type of carcinoma of the esophagus which grows through the esophageal wall, forming a mediastinal tumor, and which is associated with the striking absence of dysphagia. It was felt that such was the lesion in this case prior to the results of biopsy.

It is possible that sarcoma of the esophagus is more prevalent than would appear from their scarcity in the literature. The case of French and Garland diagnosed as carcinoma on biopsy, and at autopsy found to be a leiomyosarcoma, is illustrative of the fact that the possibility of sarcoma should be seriously considered in all cases that present filling defects due to polypoid growths in the esophagus. This is especially true where there is ulceration and infiltration into the adjoining tissues producing a mediastinal tumor mass, frequently spherical in configuration as was described in 2 of the 6 recorded cases. The fact that these lesions can simulate primary mediastinal tumors with the absence or the presence of a minimal degree of dysphagia as seen in this case, reaffirms the importance of routine roentgen esophageal examination in all mediastinal tumors.

SUMMARY

A rare tumor of the esophagus, a leiomyosarcoma involving the middle and lower third, is added to the five cases already recorded in the literature. The extension of the esophageal tumor into the mediastinum simulating a primary mediastinal tumor and the absence of dysphagia when the patient was first seen are the outstanding features of this case.

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OSTEOPOIKILOSIS ASSOCIATED WITH BRONCHOGENIC CARCINOMA AND ADENOCARCINOMA OF THE STOMACH*

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CINCINNATI, OHIO

OSTEOPOIKILOSIS and its association with other disease processes, particularly those affecting tissues of mesodermal origin,[1] has been the subject of rather infrequent, but extensive, clinical and roentgenologic reports. These have recently been summarized by Hinson.[2] This rare familial anomaly, which affects most bones of the body except those of the skull, is usually characterized by multiple areas of bony condensation in the epiphyses and metaphyses. Detailed histolopathologic description of completely autopsied cases is limited to that reported by Schmorl[6] and that by Windholz.[9] Other cases with incomplete microsopic descriptions are cited by von Stubenrauch.[7] We have been unable to find any reported cases of osteopoikilosis associated with carcinoma.

REPORT OF CASE

Hospital Number AA. 189. A single white male, aged seventy, upholsterer, was admitted to the Cincinnati General Hospital, on March 20, 1940, with a chief complaint of productive cough. The onset of his first symptoms, weakness, malaise, and easy fatigue, was in July, 1939. These persisted, and three months later he developed a cough productive of large amounts of occasionally blood-streaked, mucopurulent sputum, and a severe, rather constant, sharp, non-radiating pain in the left shoulder, made worse by cough and change in position. Because of the persistence and progression of these symptoms he was unable to continue his occupation. In December, 1939, and February, 1940, he had a shaking chill. There was no history of night sweats or fever, and there was no known contact with tuberculosis. He lost 35 pounds in weight from October, 1939, to March, 1940. For the five years preceding admission he had slight dyspnea on exertion.

Past History. The patient stated that he had always been in good health except for gonorrhea and a penile lesion contracted in 1900. The latter was treated by cauterization.

Physical Examination. Temperature, 98.2° F.; pulse, 86; respirations, 22; and blood pressure, 120/70. The patient was a well developed, moderately undernourished, aged white male. The significant findings were confined to the chest. The trachea was deviated slightly to the left. Percussion dullness with slight increase in breath sounds was present over the left apex, anteriorly and posteriorly. The remainder of the lung fields was clear to auscultation and percussion. The cardiac apex impulse was within the nipple line, and the heart was not enlarged to percussion. The heart sounds were distant and no murmurs were heard. The cardiac rate at the apex was 86 and the rhythm was regular. There was moderate peripheral vascular sclerosis. Examination of the abdomen revealed that the inferior border of the liver extended 2 cm. below the right costal margin. There were marked varicosities of the veins of the legs with an associated eczematoid rash.

Admission laboratory examinations revealed 12 gm. of hemoglobin (Sahli); 4.47 million erythrocytes and 6,400 leukocytes with a differential leukocyte count of neutrophils 68 per cent, basophils 1 per cent, eosinophils 2 per cent, lymphocytes 23 per cent, and monocytes 6 per cent. Platelets were normal. Urine and stool examinations were negative. Blood urea nitrogen, 14 mg. per 100 cc. Standard Wassermann and Kahn serologic tests were negative, but the blood Kahn test performed with sensitized antigen was 3 plus.

Dr. E. C. Elsey's roentgenological report reads: "Chest teleroentgenogram (Fig. 1)—The bony framework of the chest is abnormal in that numerous small circumscribed areas of in-

* From the Percy Shields Laboratory of the Hamilton County Tuberculosis Hospital, Dr. John Skavlem, Medical Director (a subdepartment of the Department of Medicine, College of Medicine, University of Cincinnati), Cincinnati, Ohio.

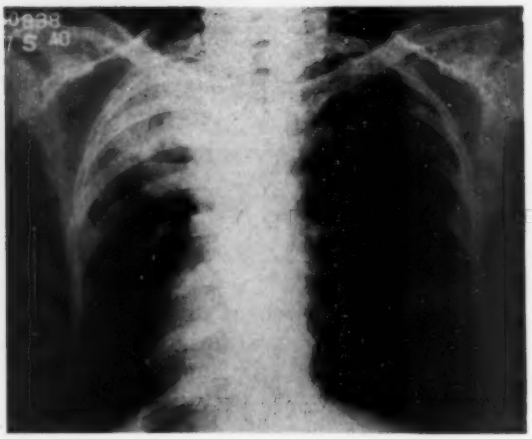

FIG. 1

creased density are present in the heads of the humeri and in the acromion processes. The trachea is deviated to the left, and the left hilar shadow appears to be higher than the right. There is a large homogeneous area of increased density in the left apex in which there is a smaller circumscribed area of decreased density. There is also a suggestion of a fluid level in the first interspace area on the left. There appears to be some emphysema bilaterally in the bases. Several calcified nodules are seen in both hilar shadows and in the right second interspace. The heart is not enlarged. The changes in the left apex may represent a neoplasm with atelectasis plus several abscesses, or a tuberculous process with cavitation, or a lung abscess with fibrosis.

"Skeletal roentgenograms (Fig. 2, 3 and 4)—The skull and mandible are essentially negative. Anteroposterior and lateral views of the cervical spine show some demineralization, and there is

FIG. 2

FIG. 3

rather marked bony lipping, which is thought to be due to hypertrophic arthritis. There may be a few circumscribed areas of increased density in the transverse processes of the cervical vertebrae, but these are not very definite and no lesions are demonstrable in any of the vertebral bodies. The pelvis shows a symmetrical distribution of small circular and ovoid densities in the ilium, ischium, pubis and about the acetabulum. The head, neck, and trochanters in both femora, the small bones of the wrists, ankles, hands, feet, and remaining long bones are similarly involved. These findings are characteristic of osteopoikilosis."

In view of these findings, the following procedures were done. Three sputum smears, negative for acid-fast bacilli, revealed gram-positive cocci. Blood serum calcium was normal. Bronchoscopy, done by Dr. Samuel Iglauer, on

FIG. 4

March 26, 1940, was significant only in that the left main stem bronchus was congested and covered by a small amount of bloody purulent material which on smear revealed occasional gram-positive cocci, and no acid-fast bacilli. An aspiration lung biopsy was attempted in the third left interspace, posteriorly. After entering the pleura, the needle encountered a very tough mass only slightly less firm than cartilage. No material or fluid could be aspirated for cytologic study.

The patient was transferred to the Hamilton County Tuberculosis Hospital on April 23, 1940, for further study and observation. The diagnoses at the Cincinnati General Hospital were bronchogenic carcinoma with abscess formation or chronic fibroid pulmonary tuberculosis with cavitation, and osteopoikilosis.

Upon admission to the tuberculosis hospital, the history and physical findings were as previously noted Stereoscopic chest roentgenogram was read by Dr. John H. Skavlem as follows: "Bony framework—Areas of decreased density are seen in the scapulae and in the heads of the humeri. The diaphragm is low in position. The heart is normal, and the aorta is obscured. The trachea is slightly dislocated to the left. A few small areas of calcification are seen in the right hilum. Right lung: Emphysema is present. A large area of calcification is seen beneath the third rib, axillary line. Left lung: The pleura is heavily thickened over the upper lobe. Two moderately large cavities are seen beneath the fourth and fifth ribs, posteriorly. These are surrounded by fibrosis and thickened pleura. Emphysema is present in the base.

"Diagnosis: The most probable diagnosis is pulmonary tuberculosis, which, however, cannot be positively made from this roentgen study alone. These changes may be due to other destructive lesions, such as cystic disease or abscess. If the sputum is persistently negative the diagnosis of tuberculosis should be questioned. In comparison with films taken on April 24, 1940, there has been no extension of the lesions." Subsequent stereoscopic chest roentgenograms revealed very little change.

Sedimentation index (Westergren method) varied between 111 on admission and 127 shortly before death. Standard Kahn and Hinton serologic tests were negative. Numerous concentrated smears of the profuse, mucopurulent sputum were negative for acid-fast bacilli. Animal inoculations and cultures for tubercle bacilli were not done.

Persistence and progression of all symptoms characterized his course in the hospital. During the last month of life, dysphonia developed. Laryngoscopic examination revealed paralysis of the left vocal cord. Eight days before death the temperature rose to 101.5° F., and the patient became confused, complained of dysphagia and retrosternal pain. Examination revealed cyanosis and evidence of marked pulmonary congestion. He died at 3:10 A.M. on November 22, 1940, seven months after admission to this hospital, and approximately fourteen months after the onset of his respiratory symptoms. The final clinical diagnoses were: Far advanced pulmonary tuberculosis and osteopoikilosis.

Necropsy T-40-76; Dr. D. Oscherwitz; eighty-four hours postmortem. The body was that of a well developed, markedly emaciated white male approximately sixty years of age. There was clubbing of the fingers and toes. Removal of the symmetrical breast plate revealed the thoracic viscera to be in their normal positions and relationships. The costal cartilages were calcified. There were focal right white fibrous pleural adhesions. The apex of the left upper lobe was covered by very dense, gritty, yellowish-white pleura measuring 7 mm. in thickness. This was extremely adherent to the chest wall and to the arch and first portion of the thoracic aorta. No fluid was present in either pleural cavity. The lungs and trachea, removed intact, were dissected after fixation in formalin and weighed 1,200 and 900 grams, left and right, respectively.

The left lung was of normal contour and lobation. The interlobar fissure was inseparably fused by firm white fibrous adhesions. To palpation the lower lobe was generally subcrepitant and contained a large cystic-like area. The upper lobe was firm throughout. Dissection of the lung by tracing the bronchial tree revealed a large cavity, measuring 10 cm. in diameter, occupying the greater portion of the lower lobe. This cavity was filled with mushy, reddish-brown material, had a trabeculated shaggy wall and was surrounded by a rim, 3 to 4 cm. in thickness, of coarsely lacy, moist, grayish-brown lung substance. The coarsely lacy tissue of the lingual tip was streaked with white fibrous bands and contained several small firm white nodules. The remainder of the upper lobe presented a large trabeculated cavity, 8 cm. in diameter, partially filled with cheesy, brown-

FIG. 5. Frontal section of the posterior portion of the left lung.

ish-yellow material. The wall of this cavity was thick, firm, rubbery, streaked with black fibrous bands, and studded with firm yellow nodules, the larger of these being 3 cm. in diameter. The main upper lobe bronchus was dilated, thickened, and abruptly opened into the cavity (Fig. 5). A small area of coarsely lacy, crepitant lung tissue remained at the anterior margin.

The right lung was of normal contour and lobation. To palpation the entire lung was subcrepitant except for a small, hard, subpleural density on the lateral aspect of the upper lobe. Dissection of the lung by tracing the bronchial tree revealed coarsely lacy, grayish-brown lung substance. A calcified, irregular nodule 1 cm. in diameter, probably a Ghon lesion, was present in the substance of the upper lobe. Sparsely scattered throughout, particularly in the subpleural tissue of the lower lobe, were small, irregular whitish areas of increased density. The bronchi were normal.

The moderately enlarged tracheobronchial lymph nodes on section presented either firm or soft anthracotic substance. Some of these were enclosed by a thin yellowish-white zone, and others had focal areas of calcification.

The aorta, of normal caliber, was lined by a generally smooth intima. In the region of the dense pleural adventitial adhesions there were numerous umbilicated yellowish intimal plaques. The esophagus was normal.

The stomach was lined by a generally smooth, grayish-white intact mucosa. A flat, firm, intramural, indefinitely demarcated yellowish mass, approximately 4 cm. in diameter, was present in the prepyloric region.

A soft, yellow, poorly defined nodule, 2.5 cm. in diameter, was present in the right kidney parenchyma adjacent to the inferior portion of the pelvis.

Portions of the right ilium, the superior ramus of the right pubis, the left greater trochanter, the distal phalanges of the left foot, the distal end of the right radius, and several of the right carpal bones had a coarsely trabeculated, yellow marrow. That of the skull, ribs, sternum and lumbar vertebrae were grossly normal.

Microscopic examination revealed that the normal structure of the upper lobe of the left lung was extensively replaced by necrotic neoplastic tissue which was confluent about and formed the wall of the large cavity. The distal portion of the bronchus communicating with the latter was densely infiltrated by clumps of tumor cells. Focal areas of subpleural alveoli were lined by or filled with well preserved neoplasm. There was an associated marked collagenous thickening of the pleura, pleural septa, and coarse fibrous bands permeated the entire tumor. Thrombi of neoplastic cells were present in an occasional artery in the necrotic substance; other vessels showed moderate atherosclerosis and neoplastic invasion of their walls. The tumor consisted of sheets, strands, and clumps of generally large, polyhedral, acidophilic cells, having either round or oval, pale nuclei with prominent nucleoli, or irregular hyperchromatic nuclei in various stages of mitoses. Frequently these cells were arranged concentrically about keratinized centers. Metastases, having the same structure, were present in the right kidney (Fig. 6), pancreas, and several abdominal peri-aortic lymph nodes. There was direct extension to the mediastinal pleura and adherent aortic adventitia. Sections of the right lung, and remaining portions of the left, revealed discrete and confluent acute lobular

pneumonia with abscess formation in the left lower lobe. A healed primary tuberculous complex was present on the right.

Decalcified sections of skull, ribs, and lumbar vertebrae were normal. Those of the right ilium, left greater trochanter, distal end of the right radius, a phalanx of the left second toe, and several of the right carpal bones revealed normal cortices and subcortical studding of the medullae with large, irregular osseous masses. These were composed of thickened, apparently fused trabeculae which surrounded small islands of fatty marrow. These osseous foci, in general containing Haversian systems, had peripheral radiations of normally lamellated, thickened, irregular trabeculae. In some areas the latter were

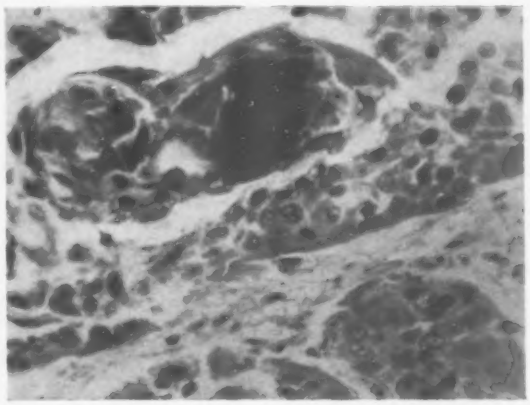

Fig. 6. Photomicrograph of metastasis to right kidney. Trichrome stain. ×375.

continuous with the cortex, and in others with the spicules of other nodules. Throughout the subcortical region there also were normal and thickened, ocasionally clubbed, irregular trabeculae. A small focus of active fibrosis of the marrow with slight osteoclastic activity was present in one of the osseous masses. The normal diaphyseal and abnormal subcortical cancellous bone blended imperceptibly (Fig. 7).

Microscopically, the mucosa of the thickened portion of the stomach consisted of sharply alternating areas of normal and neoplastic tissue; the latter extensively invaded the submucosa, muscularis, and subserosa. The tumor cells were arranged in clumps, strands, small acini, and focally, in the mucosa and submucosa, presented areas of colloid change (Fig. 8). Generally, these cells were polygonal with finely granular, vacuolated, eosinophilic cytoplasm and hyperchromatic oval nuclei, occasionally in

Fig. 7. Trichrome stain. Decalcified. ×33.

mitoses. In and about the colloid areas there were numerous signet ring cells. Throughout there was a moderate increase in collagen which was focally infiltrated with lymphocytes. Sections of other portions of stomach were normal. No metastases of this colloid adenocarcinoma were found.

The important pathological diagnoses were: Squamous cell bronchogenic carcinoma of the left upper lobe with marked tumor necrosis, extension into the pleura and aortic adventitia, and metastases to the right kidney, pancreas and abdominal peri-aortic lymph nodes; extensive bilateral confluent lobular pneumonia with abscess formation in the left lower lobe; colloid adenocarcinoma of the stomach; osteopoikilosis.

COMMENT AND SUMMARY

The abnormal densities in the bones of the shoulder girdle were noted in the first

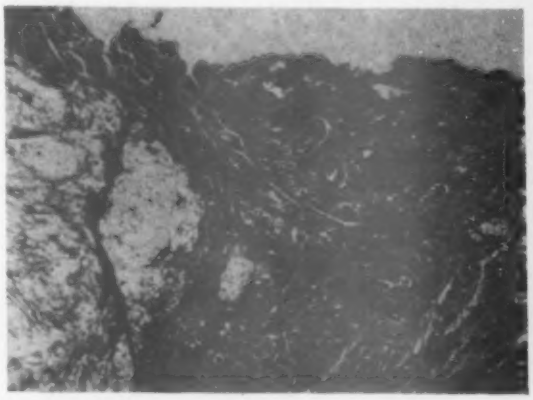

Fig. 8. Trichrome stain. ×33.

chest roentgenogram. The possibility of confusing these bony changes with those produced as a result of metastases from a lung carcinoma was obviated by subsequent roentgen examination of the entire skeleton which revealed the typical symmetrical wide spread involvement of osteopoikilosis. As in many of the reported cases, this condition was disclosed by roentgenograms made for other purposes. This patient had no living relatives; however, several roentgen studies have shown that it is a familial, apparently recessive and non-sex-linked asymptomatic anomaly.[2] During the short period of observation of this patient, no change in size of these osseous densities was noted on serial roentgenograms. The gross and microscopic findings were similar to those previously reported and contribute nothing to the possible etiology of this condition. The parathyroids were not examined and a single blood calcium determination was normal.

The important clinical problem in this case was that of differential diagnosis between tuberculosis and carcinoma of the lung. The initial occurrence of a chronic lung disease in an elderly white male with no previous history of tuberculosis should be more suggestive of a neoplastic rather than a tuberculous process, particularly in view of the fact that the unfavorable course was associated with stationary lung roentgen findings and failure to demonstrate tubercle bacilli. The problem of bronchogenic carcinoma masquerading as tuberculosis or other chronic lung disease has been discussed by Ritterhoff[5] and Middleton.[4] Occasionally tuberculosis and carcinoma of the lung may coexist and only by extensive laboratory procedures and their proper interpretation can this be determined.

The association of a primary bronchogenic carcinoma with a primary adenocarcinoma of the stomach is relatively uncommon.[8] The average incidence of multiple primary tumors is approximately 4 per cent of cancer cases.[3,8]

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ROENTGENOLOGICAL REPORT OF CHEST EXAMINATIONS

MADE OF REGISTRANTS AT U. S. ARMY INDUCTION STATION NO. 6, THIRD CORPS AREA, BALTIMORE, MARYLAND, MAY 1, 1941 TO MARCH 31, 1942*

By HOWARD E. ASHBURY, *Lieutenant Colonel, M. C., U. S. Army,*
JAMES G. WHILDIN, *Captain, M. C., U. S. Army, and*
FRANK T. ROGERS, M.D., *University of Texas, Galveston, Texas*

THE original report of our roentgenological chest survey was published in this JOURNAL in August, 1941.[1] At that time we reported 11,870 chests examined at the U. S. Army Induction Station No. 6 between November, 1940, and April 30, 1941.

For the present report we have selected 22,054 chests, examined at the same station between May, 1941, and March 31, 1942, making a total of 33,924; of this number 18,000 were made with paper films by Powers Survey Corporation under contract with the Army.

The films were read by the radiological members of the examining board, namely: Lieutenant Colonel Howard E. Ashbury, M. C., Dr. Webster H. Brown, Dr. John Evans, Dr. Whitmer B. Firor, Dr. Eugene L. Flippin, Dr. Walter L. Kilby, Dr. Frank T. Rogers, Dr. Henry J. Walton, and Dr. Harold E. Wright.

The Army Photo-Roentgen Unit was installed and put in operation at this station in September, 1941, under the direction of Captain James G. Whildin; 15,924 selectees were examined between September 1, 1941, and March 31, 1942, using 4 by 5 inch stereoscopic films supplemented by 14 by 17 inch stereoscopic films whenever a decision could not be made from the 4 by 5 inch films alone. This is probably the most ideal setup available at this time. The vast improvement in quality and the thoroughness of the examination by this method should give an almost perfect score for interpretation, and yet it is realized that there are still a number of undiagnosable lesions getting by the examining board, to be picked up later in the hospitals. The term "diagnosable lesion" refers to lesions that can be visualized and interpreted by a qualified roentgenologist. There is, however, a group which cannot be diagnosed under the best of working conditions because they have not developed to a recognizable stage of the disease when the men's chests are roentgenographed.

White[5] in his report of 40,000 films made for the Australian Imperial Forces mentioned this difficulty too. He says: "It must be stressed that radiological examination, no matter how carefully it is carried out and no matter what technical method is employed, is not absolutely fool proof. I have knowledge of at least six patients whose original skiagrams showed no abnormal shadows, yet, whose sputum contained tubercle bacilli." At the present time we have a most enlightening case who has a fulminating infection which will cause his death in a few weeks. Review of the initial paper film in this case reveals a normal roentgenogram; those taken a few months later show an advanced bilateral pulmonary tuberculosis. In order to avoid this sort of thing and to eliminate those men who may develop a small initial lesion a short time after induction, the Australians are now using a more elaborate and time-consuming method of examination. This consists of photo-roentgenographic examination, tuberculin test, a most complete history and a stomach washing for bacterial study. This sounds involved but actually consumes only three days.

Webster[4] in his work correlating his

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roentgenological and bacteriological findings reports that in 125 men with roentgen diagnosable lesions 83 (53 per cent) were positive to bacteriological tests. Of 90 men reported healed roentgenographically, 10 gave positive bacteriological results. Most surprisingly, of 3 men reported negative by roentgen findings all were found positive to bacteriological culture. It would seem then that in civilian practice our ideas of so-called carriers will have to be changed, and physicians will have to realize that a negative sputum by the usual staining methods is not sufficient proof that the patient is not discharging the organism. Stomach washings and culture are necessary in certain groups of cases if we are to exclude all cases of pulmonary tuberculosis.

TABLE I

TOTAL NUMBER OF CHEST ROENTGENOGRAMS		22,054
Chest roentgenograms negative	18,883	
Anomalies of heart, lungs, and chest wall	270	
Non-tuberculous conditions	105	
Pulmonary tuberculosis		
Primary tuberculosis	2,551	
Reinfection	245	
		22,054
Disqualifying lesions		
Cardiovascular lesions	24	
Acute respiratory infection	10	
Spontaneous pneumothorax	2	
Pulmonary tuberculosis	294	
Other chest conditions	27	
TOTAL	357	
ACCEPTED	21,697	
		22,054

The work done so far by the Army Examining Boards has shown clearly the necessity for roentgenographing the chest of all selectees, recruits, applicants for commissions, in all branches of the service; in addition, whenever a soldier changes status, requiring a physical examination, the chest should be roentgenographed. It is our understanding that this is now being done in our Army.

We are not informed at present as to just how much pulmonary tuberculosis is being missed by the examining boards but we are aware that there are occasional requests for films of men in hospitals who have developed a pulmonary lesion, after they have been passed by the examining board. This occurs usually several months following induction, and so far has been confined to earlier examinations. We have not, to the best of our knowledge, had any examinations made with the 4 by 5 inch films come back to plague us, but we will certainly have a few later on.

Following the same classification which we used in the original report,[1] we see that fewer anomalies were reported and there is a definite decrease in the non-tuberculous conditions; this latter difference may be seasonable. There is a definite increase in the number of cases of pulmonary tuberculosis; note the increase reported on the 4 by 5 inch films, which we think is due to the fact that all films showing calcification were reported and in the first survey they were not.

Of the 22,054 men examined roentgenographically in this series, we find 2,551 cases of primary tuberculosis and 245 cases of re-infection tuberculosis, or a total of 2,796 cases; about 13 per cent with roentgenographic evidence of disease, an incidence of about 3 per cent greater than in the original survey.

Of this group 294 were rejected (1.3 per cent) for pulmonary tuberculosis, an increase over the last survey of 0.1 per cent. Of the cases examined on paper films 1.2 per cent were rejected, while of those examined with the 4 by 5 inch films supplemented by 14 by 17 stereoroentgenograms, there were 1.3 per cent rejected which we interpret as being due to greater efficiency of this method.

The primary tuberculous lesions (2,551) consisted of healed miliary, excessive calcification, stable or unstable, as evidenced

TABLE II

SURVEY OF 22,054 CHEST ROENTGENOGRAMS OF INDUCTEES
U. S. ARMY INDUCTION STATION NO. 6, BALTIMORE, MARYLAND
May 1, 1941 to March 31, 1942

Thoracic cage — anomalies	Cervical ribs		21	
	Bifid ribs		64	
	Rudimentary ribs		27	
	Scoliosis		84	
	Spina bifida		5	
Thoracic cage — fractures	Synostosis		21	
	Ribs		12	
	Clavicle		5	
Lung anomalies	Accessory lobes		5	
	Azygos lobes		30	
Heart anomalies	Dextrocardia		8	
	Miscellaneous		5	
Heart and great vessels	Organic disease		24	
Foreign body			11	
				322
Tuberculosis	Primary	Outer zone calcification (Ghon tubercles)	191	
		Midzone calcification	249	
		Tracheobronchial glands	11	
		Hilar glands	2,006	
		Miliary tuberculosis, healed	48	
		Pleural cap	46	2,551
	Adult Reinfection	Minimal: in excess of minimal	116	
		Moderately advanced	123	
		Far advanced	6	
		Cavitation (17)		245
Pleurisy	Recent		2	
	Residual		18	
Empyema	Residual		6	26
Non-tuberculous conditions	Bronchitis chronic*		2	
	Bronchitis chronic with emphysema*		6	
	Acute respiratory (bronchopneumonia)		8	
	Spontaneous pneumothorax		2	
	Diaphragmatic anomaly		1	
	Mediastinal tumor		3	
	Pneumoconiosis		2	
	Mediastinal hernia		1	
	Atelectatic accessory lobe		1	
	Grossly deformed chest		1	27
Chests	Negative			18,883
				22,054
Accepted				21,697
Disqualified				357
				22,054

* A roentgen diagnosis of chronic bronchitis is only made when substantiated by physical findings.

by stippling, soft tissue proliferation and increase in size or number of the glands and parenchymal lesions. Where instability was the only cause for rejection re-examination was advised after a six months' interval. When there is no evidence of progression or regression the case is accepted.

TABLE III

TOTAL NUMBER OF MEN EXAMINED AT U. S. ARMY INDUCTION STATION NO. 6 AND NUMBER OF SELECTEES WHO WERE REJECTED FOR TUBERCULOSIS FROM MAY 1, 1941 TO MARCH 31, 1942

Month	Men Examined	Rejected for Pulmonary Tuberculosis	Per Cent
May, 1941	3,488	38	1.1
June, 1941	2,373	28	1.2
July, 1941	1,894	13	0.7
August, 1941	1,195	9	0.75
September, 1941	1,876	26	1.38*
October, 1941	2,632	44	1.6
November, 1941	716	12	1.6
December, 1941	1,726	24	1.4
January, 1942	3,100	34	1.09
February, 1942	1,151	21	1.8
March, 1942	1,903	45	2.3*
GRAND TOTAL	22,054	294 Average	1.33

* 4 by 5 inch films were used from September, 1941 to March 31, 1942.

The reinfection tuberculous lesions (245) consisted of minimal, moderately advanced and far advanced cases. There were 17 cases with cavitation (5.7 per cent), less than the first survey by 1.3 per cent.

All cases rejected for tuberculosis were reported to the Maryland State Board of Health for follow-up care.

Following the first survey, the Maryland Tuberculosis Association arranged for facilities to roentgenograph the chests of selectees for the local boards so a large percentage of cases with tuberculosis did not reach the Army Examining Board (they all do now). This also occurred in quite a number of instances in the first survey, so the figures are balanced.

A Board of Review of Chest X-Rays was set up by the Medical Director, Maryland Selective Service System, consisting of two radiologists and a tuberculosis specialist to review the roentgenograms made for the local boards, namely, Dr. Whitmer B. Firor, Dr. Walter L. Kilby, and Dr. Victor S. Cullen. The chief radiologist to the Army Examining Board was invited to sit with this board. The following quotation from Circular Letter #429 Selective Service Headquarters indicates the value of the work of this board (Table IV):

The review of chest cases in compliance with the provisions of Circular Letter #395 and 413 has resulted in the reclassification of approximately one-half of the cases studied, from Class IV-F to Class I-A. The salvage of such a high percentage of men for general military service shows that the effort has been worth while. For this reason it is desired to make the practice of reviewing such cases a continuous process, and to continue to have reviewed the films of those classified in Class IV-F on x-ray evidence alone.

TABLE IV

REPORT OF BOARD FOR REVIEW OF CHEST FILMS OF CASES CLASSIFIED IN CLASS IV-F FOR TUBERCULOSIS ON ROENTGEN EVIDENCE ALONE

Number of cases reviewed	750
Number of cases classified in Class I-A	207
Number of cases with borderline lesions classified in Class I-A for final determination at Induction Station	76
Number of cases on which Medical Advisory Board study was recommended	36
Number of cases continued in Class IV-F	331
Percentage of cases classified in Class I-A	31.8
Percentage of cases with borderline lesions classified in Class I-A for final determination at Induction Station	11.7
Percentage of cases to be sent to Induction Station	43.5
Percentage of cases on which Medical Advisory Board study was recommended	5.5
Percentage of cases continued in Class IV-F	50.9

The roentgenograms reviewed were taken during the period of November 25, 1940 to February 28, 1942.

We have listed in Table III, the number of inductees examined each month, with the rejections for tuberculosis. This averages 1.33 per cent, a little greater than the previous survey, but quite close.

We are especially indebted to Lieutenant Morris Bastacky of Pittsburgh, Pennsylvania, for his valuable assistance in checking the statistical data.

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THE USE OF DIODRAST IN DETERMINING THE LOCATION AND EXTENT OF PULMONARY EMBOLISM

AN EXPERIMENTAL STUDY*

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ACCORDING to Barnes,[1] approximately 33,000 people die yearly from pulmonary embolism. At this rate it can be estimated that 3,000,0000 persons now living in the United States may eventually succumb to it. Belt[2] finds pulmonary emboli in 10 per cent of his autopsies, and several others report equally high proportions of pulmonary embolism following operation.

As early as 1908, Trendelenburg,[20] suggested a method for dealing with this dreaded surgical complication. Although an extremely risky procedure, when performed in time embolectomy (Trendelenburg operation) is life saving in the majority of cases. At present there are more than ten successful removals of pulmonary emboli on record.[18] It is readily seen that compared to the incidence of pulmonary embolism, embolectomy has hardly been given an opportunity to demonstrate its efficacy.

Why then has such a promising procedure been used so rarely? A large majority of postoperative pulmonary emboli are of the non-fatal type, usually distinguishable from fatal emboli only by the severity of the symptoms. Most surgeons hesitate to subject a patient to an embolectomy if they feel he has any chance of surviving without it, and so, in many instances they wait until it is too late. We believe that if the surgeon could know beforehand, with a fair degree of accuracy, whether the embolism is likely to be fatal, embolectomy would be tried more often with success. It is important, therefore, to visualize the extent and location of the pulmonary embolus. To facilitate this, one of us (I.R.L.) suggested the use of a non-toxic radiopaque substance (diodrast) to be injected into the venous circulation. Roentgenograms are taken of the opaque medium as it fills the pulmonary arteries, with the idea in mind that an occluded vessel cannot fill with diodrast and cast a corresponding shadow.

In order to test the accuracy of this method we had first to experimentally produce an embolus in an animal which would simulate that occurring in man.

Virchow,[23] as early as 1856, inserted rubber balls into the peripheral veins of animals, occluding the pulmonary vessels. Since then a great variety of substances have been used for this purpose, such as paraffin balls;[7,10,16,21] mercury;[24] blood clots;[12,14,15] starch grains,[4] or starch suspension,[8] lead shot and lead dust;[19] plant seeds;[3,13] lipiodol and other oils;[6,11] mucilage;[22] vaseline;[9] bismuth,[5] and a mixture of barium sulphate, ferric chloride, and sodium chloride.[17] In spite of the diversity of these methods, practically all had this in common: the substance was injected or inserted into a vein. In 1920, however, Dunn[8] injected a starch suspension directly into the right ventricle of goats. In our studies we also injected directly into the right side of the heart.

Our first problem was the choice of a non-toxic opaque material to produce the embolus. This had to be fluid enough to pass through a needle, and yet solid enough to form one large embolus. Several materials were tried, with the procedure as follows:

* Approved for publication by the Surgeon General, U. S. Public Health Service.

A No.18 gauge gold needle, filled with the required amount of embolus-producing substance, was put through the chest wall immediately overlying the right ventricle of a rabbit, anesthetized with sodium phenobarbital. A stylet was employed to empty the needle, and the progress of the embolus through the pulmonary artery noted under roentgenoscopy.

We used different embolus-producing substances, such as lead filings, iron filings, and mercury, each mixed with low melting point paraffin to give the mixtures softer consistency. Lead filings gave the most satisfactory results. When a non-opaque embolus was desired, the paraffin alone was used.

Once the embolus was produced, our next problem was to see if it could be located by the use of diodrast. When opaque emboli were used, we could, of course, locate them with ease roentgenographically. In these cases we noted the

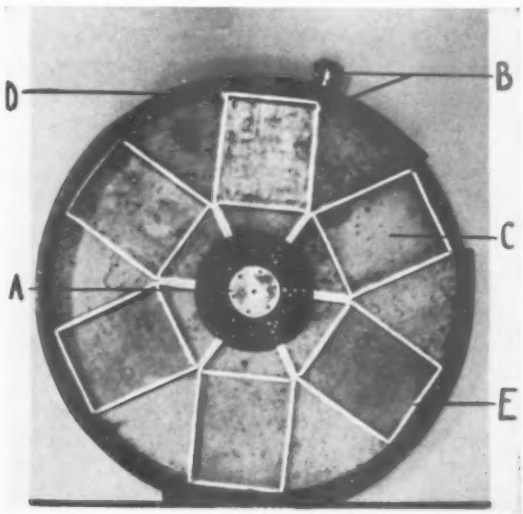

Fig. 1. Under-side view of plate-changer. *A*, spring motor; *B*, magnetic release; *C*, leadless area; *D*, back-stop; *E*, trays for film cassettes.

absence of filling of the pulmonary arteries below the embolus. This became the significant point looked for in determining the size and location of the non-opaque emboli which were later produced.

Since in any particular case the exact moment of maximum filling of the pulmonary arteries with the diodrast is not known, it was found necessary to take several roentgenograms in a short period of time, so that at least one of them would be exposed at the right instant. To accom-

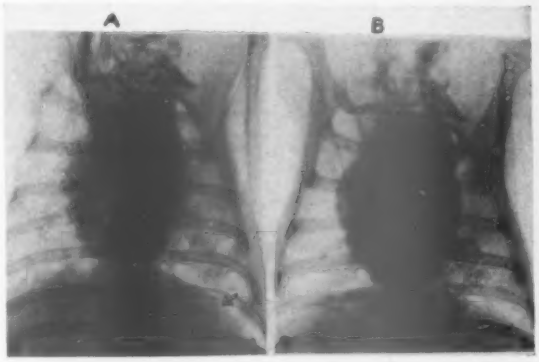

Fig. 2. Diodrast roentgenograms before (*A*) and after (*B*) embolization. A definite vascular loop is seen in left base (*A*), the lower arch being indicated by arrow. After embolization (*B*) the lead filings along the obstructed vessel can be seen up to the point of total occlusion. The lower arch seen in (*A*) is absent.

plish this we had to develop a plate-changer which permitted taking as many as six roentgenograms in six seconds.

This plate-changer (Fig. 1) resembles, in effect, a large spring-driven phonograph turn-table, 44 inches in diameter, with trays for 8 by 10 inch film cassettes occupying six positions on the circumference of the rotating disc. The mechanism also contains a magnetic release, and a ratchet stop to prevent the trays from vibrating after they have been moved into position. The entire machinery is covered by a flat circular board lined with lead in all but one 8 by 10 inch area, which exactly overlies the 8 by 10 inch film which is being exposed. This area is hinged for the purpose of inserting the cassettes.

The diodrast was injected into the marginal vein of the animal's ear, and six roentgenograms were taken of the chest in less than eight seconds. This method was found entirely satisfactory. The diodrast clearly demonstrated the position of the

embolus, even in the smaller branches of the pulmonary artery. Figures 2 and 3 show such diodrast roentgenograms, before and after the embolization. Note the filling of the branch of the pulmonary artery before the obstruction was produced (arrow) and the absence of filling after the occlusion, showing that diodrast effectively located the point of obstruction.

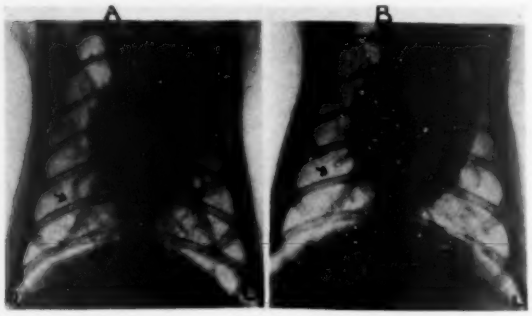

FIG. 3. Diodrast roentgenograms before (*A*) and after (*B*) embolization. Note abrupt cessation of diodrast shadow indicated by arrow at point of obstruction in (*B*).

By changes in the construction of the plate-changer it is proposed to apply the method to man. In a postoperative attack suggesting embolism it should be simple for a competent roentgenologist to determine whether any of the large branches of the pulmonary artery are occluded. If the embolus is too small for its effects to be seen (i.e. less than a lobar branch) the patient will probably recover. If, however, the entire right pulmonary artery is obstructed, then the surgeon could operate on the patient, feeling relatively confident that he has little chance to survive without an embolectomy.

The advantage of the diodrast roentgenogram over the ordinary roentgenogram is fairly obvious. Pulmonary embolism is determined from the roentgenogram by the presence of an infarct, and this does not show roentgenographically until at least twenty-four hours after the attack. With the diodrast film, action can be taken immediately after the attack, and surgical intervention may be employed before the heart is too weak to recover.

SUMMARY AND CONCLUSION

The high percentage of deaths from pulmonary embolism emphasizes the need for a clinical method of determining the size and position of the embolus. To study this experimentally a solid embolus was first produced in the rabbit's lung. The diodrast method was found effective in visualization of the pulmonary arteries up to the occlusion, so that the extent of the embolus could be determined roentgenographically without harmful effects. The diodrast is injected into a peripheral vein, and six chest films are taken within six to eight seconds following the injection, by the use of a specially constructed plate-changer. The method should be applicable to postoperative embolism in man, since emboli large enough to cause serious damage can easily be identified by this means.

We wish to thank Dr. William Y. Hollingsworth for his stimulating influence during these experiments, and Mr. George Allen for his cooperation in the animal experiments.

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MICROCEPHALY FOLLOWING MATERNAL PELVIC IRRADIATION FOR THE INTERRUPTION OF PREGNANCY*

REPORT OF A CASE

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SINCE the time when it was discovered that the rays of radium and of the roentgen tube can influence biological processes, the possibility that exposure of the human ovaries before conception, or of the fetus in utero might be injurious, has been a matter of concern to radiologists, obstetricians and gynecologists.

Existing knowledge regarding this relationship can be summarized under the following headings:

(*A*) Therapeutic roentgen and radium irradiation of the ovaries prior to conception.
(*B*) Diagnostic roentgen exposure of the fetus in utero.
(*C*) Therapeutic roentgen and radium exposure of the fetus in utero.

(*A*) *Therapeutic Roentgen and Radium Irradiation of the Ovaries Prior to Conception.* The amounts of radium and roentgen irradiation commonly employed for the treatment of lesions in the maternal pelvis during the child-bearing period may produce: (*a*) no effect on ovulation; (*b*) temporary, or (*c*) permanent sterility. Numerous infants have been born following a preconception, maternal pelvic irradiation which produced temporary sterility.[3,4,5,6,9,10,11,12] There is no evidence to indicate that such treatment has any deleterious effect upon either the health or the development of the infants conceived subsequently. de Rényi, de Rényi and Murphy,[1] from experimental observations, explain this absence of effect on the ground that the power of the egg cell to become fertilized is its first function to be destroyed by irradiation.

(*B*) *Diagnostic Roentgen Exposure of the Fetus in Utero.* During pregnancy the chief use for diagnostic roentgen radiation lies in the field of pelvic mensuration. Exposures for this purpose usually are given relatively late in pregnancy, and of necessity are extremely short in duration. Many thousands of diagnostic exposures have been made, and thus far no evidence has appeared to indicate that such irradiation is detrimental to the infant. On the basis of this negative evidence it may be assumed that diagnostic roentgen radiation during pregnancy is harmless to the fetus in utero.

(*C*) *Therapeutic Roentgen and Radium Exposure of the Fetus in Utero.* Therapeutic amounts of radium and roentgen exposure are many times greater than those used for diagnostic purposes. Also, they are much more likely to be given, accidentally or intentionally, earlier in the life of the embryo, than those employed for diagnostic purposes. Such exposures have been followed by the birth of both normal and malformed offspring.[1,3,4,5,6,9,10,11,12] Quoting from an earlier contribution by one of us,[11] the following data were secured: Of 74 children irradiated heavily before birth, who went to term, 25 were congenitally malformed. Of the latter, 17 were microcephalic idiots. The details of the treatment of these individuals varied widely, and in some cases even were lacking. They were made before a standard of measurement for radiation

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dosage was established. In general, however, the incidence and severity of the damage to these infants was proportional to the radiation dosage and the immaturity of the the embryo.

Since the above reports were published, at least three others have appeared, indicating that microcephaly continues to occur following therapeutic pelvic irradiation.[2,7,8]

As a result of the earlier observations[1,3,4,5,6,9,10,11,12] radiologists were warned of the danger of irradiating the human embryo. In view of our lack of knowledge regarding the amount of irradiation which may be entirely harmless to the fetus, it was advised that no fetus be exposed. To avoid even accidental exposure it was further advised that a curettage should precede irradiation, and if a series of treatments were planned over a period of days, that the patient should be warned about the danger of becoming pregnant between exposures.

In view of the seriousness of prolonged exposure, it follows that no irradiated fetus should be permitted to continue its intrauterine life. If the treatment is not severe enough to produce abortion, the uterus should be emptied.

In the case which follows the embryonic irradiation was intentional on the part of both the mother and the radiologist. Abortion failed to occur and no effort was made to terminate the pregnancy before the period of viability.

CASE REPORT

Family History. The parents of the infant to be described are a Jewish couple, of about middle-class education and social-economic status. The husband is a farm school graduate; the wife had one year of high school education, and a year's attendance upon a business school course. According to the wife, there is no instance of feeblemindedness, microcephaly, or insanity in either branch of the family. Her health and that of her husband have always been good.

Maternal Reproductive History. The couple were married in 1932, the husband being twenty-four and the wife twenty-three years of age. Between May, 1933, and April, 1938, four bright, normally developed children were born. Their birth weights were respectively: 2,828 gm., 3,136 gm., 2,772 gm., and 2,880 gm. They developed normally both mentally and physically, sitting up before seven months of age, and walking before a year old. These siblings when seen by us, when the oldest was eight years old, were obviously intelligent, eagerly alert, developmentally above average, and advanced in school work.

Soon after the birth of the fourth child the mother became pregnant again. Deeming it inadvisable on physical and economic grounds to carry this child to maturity, she consulted her family physician who referred her to a roentgenologist, with the view of having the pregnancy terminated by means of roentgen irradiation.

Her last normal period occurred July 22, 1939. Approximately ten weeks later, some time in September, she received two pelvic roentgen exposures, three days apart. The details of the treatments are not available. However, the mother states that for both exposures she lay upon her back, and the roentgen tube was turned on above her. Each exposure lasted a matter of some minutes. The two exposures were sufficient to tan her skin.

Life was not felt until the seventh month of pregnancy and only feebly thereafter. The infant was born apparently at term on April 30, 1940, after a three hour labor which was uneventful. Its body measurements at birth were: Crown-heel length 445 mm.; head measurements, biparietal 90 mm., suboccipito-bregmatic diameter 95 mm., circumference 335 mm.; body weight 2,130 grams.

Infant at Fourteen and One-half Months of Age. The infant is a male weighing 4,984 grams (11 lb. 2 oz.) and is 665 mm. in crown-heel length. He is generally underdeveloped and gives the impression of being a somewhat wizened, immature child of limited mental and physical development.

General Development. Leg development is better than that of the arms. The left side of the body, however, is more poorly developed than the right, and is associated with a facial asymmetry. Mild contractures of the left arm and leg are present, associated with foot drop and inversion of the toes. The muscles generally are relaxed, but this is associated with occasional, mild generalized muscular tensions. The

left thumb is held in the fist. The infant can hold nothing in his left hand and only very small things in the right one. The fontanelles are closed.

Movements. The infant cannot sit unsupported or stand. Spinal control is definitely relaxed when he is supported in the sitting posture. When held with his feet touching the floor he makes no attempt to put them down or bear any weight upon them.

Spastic-athetoid movements of the hands and arms are present. All movements are rather jerky; voluntary coordination is rather limited except for random movements.

In the prone position he holds his head up for an indefinite period, but rather unsteadily. He cannot raise his shoulders when lying prone, rolls to one side with difficulty and is unable to turn from supine to prone.

Attention is alert, earnest and sustained for relatively long periods. The eyes follow moving objects but this is accompanied by marked turning of the head. The pupils are equal and react slowly to light and accommodation. Gross and ophthalmoscopic examination revealed no evidence of any eye abnormality.

Body Measurements. Crown-heel length is 665 mm., which is average for infants six to eight months of age. Cranial circumference is 377 mm.; longitudinal head diameter 125 mm.; head breadth 104 mm.; head height 85 mm. These are slightly above the average at birth, as given in the Quetelet tables. They are definitely below the one year norms. Cranial content is calculated at 670 cc. (Lee formula), which is average for birth according to the Porteus' Table No. 12.

Comparing the present cranial measurements with those taken at birth, there is an increase of 42 mm. in circumference, 30 mm. in longitudinal diameter and 14 mm. in transverse diameter (height not taken at birth).

The occiput is rather flat, otherwise the cranial form is good, but the volume and its relation to the facies definitely suggest microcephaly.

Mental Development. Direct examination by the Kuhlmann-Binet test for the first years of life gives a measured mental age of 5.4 months, with no tests passed above the three to six months level. The calculated I. Q. is 38 points. There is almost total absence of speech, with only limited spontaneous vocalization, and no appreciable articulation, or attempt to imitate speech. The majority of tests passed are essentially neuromuscular rather than intellectual.

Social Development. Maturation in social performance as measured by the Vineland Social Maturity Scale shows only 5 out of 17 items passed in the first year of life, and no items thereafter. The recorded score is 0.3 years, with social quotient calculated at 25 points.

Prognosis. The volume of the cranium and its relation to the facies definitely suggests microcephaly, with poor prognosis for appreciable increase in size in relation to age. Prognosis for mental development is definitely unfavorable, except for small amounts, with a consequent presumption of a declining I. Q. The relatively low score on the Vineland Social Maturity Scale, as compared with the mental scale, is interpreted as further indication of unfavorable prognosis for both mental and social development.*

DISCUSSION

The purpose of this paper is to call attention to the hazards of fetal irradiation. We are not concerned here with the moral and ethical questions that might be raised. This case does, however, emphasize the individual as well as the joint responsibilities of the patient, the consulting physician, and the roentgenologist with respect to the material consequences.

This mother might have been advised that if the pregnancy were not terminated by this means the consequences to the prospective child might be grave. Similarly, the physician consulted and the roentgenologist who administered the treatment might have insisted, once this course of action was decided upon, that the pregnancy be actually terminated—if not by the roentgen-ray exposure then by some infallible means. In the present circumstances these precautions were not observed and the responsibility for the regrettable consequences was not fulfilled. The purpose of this paper, then, is to urge the importance of protecting all concerned

* On November 22, 1941, the patient gave birth at term to a 6 pound, 8 ounce male child which appeared to be normal in every respect. Head circumference 34 cm., biparietal diameter 9 cm., suboccipito-bregmatic diameter 10.2 cm., crown-heel length 47.5 cm.

whenever fetal irradiation is involved, regardless of the immediate purpose of such irradiation.

SUMMARY AND CONCLUSIONS

An instance is reported in which a microcephalic child was born at term following pelvic irradiation given during the third month of gestation for the purpose of producing abortion.

From this study, and others previously reported, it is concluded that no human fetus should receive large amounts of radium or roentgen radiation. If fetal death or abortion does not follow such exposure immediately, the pregnancy should be terminated at the earliest suitable moment.

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CONTACT ROENTGEN THERAPY

EVALUATION OF RESULTS FROM A CLINICAL AND PATHOLOGICAL STANDPOINT*

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DEFINITION

CONTACT, or short distance roentgen therapy derives its name from the fact that the roentgen tube can be placed in direct contact with the area to be treated. Its most important implication is the shortened target-skin distance. By virtue of the inverse square law the intensity at the surface of the tube in contact with the area being treated is extremely large; as a result, the dosage gradient within tissue drops approximately 75 per cent within the first centimeter. This method of therapy is ideal where the entire effect of the rays is required superficially and where deep penetration is best avoided (Fig. 1, 2 and 3).

HISTORY

Levine, Pack and Gallo[7] have concisely described the development of contact roentgen therapy in Germany. In 1932, Schaefer and Witte[10] first suggested the practicability of a roentgen tube whose rays would have the same absorption values as radium. They thought that this method might be used within body cavities in lieu of radium. Chaoul and Adam[5] further developed the uses of such an apparatus and described a method which has since been known as the "Chaoul technique." Chaoul fractionated his treatments, using 60 kv., 0.2 mm. Cu (inherent) filtration, and a target-skin distance of 5 cm. He applied this to all topically located tumors, such as mouth, skin, cervix, uterus, and rectum.

Van der Plaats[11] believed that with such a technique it would be "impossible to obtain so steep a decrease of dose with depth as a large proportion of superficial tumors demand." He therefore used an air cooled tube with no inherent filter which allowed him to shorten the skin-target distance to 1.8 cm. These factors resulted in a further reduction of the depth dose. Pendergrass, Hodes and Garrahan[9] have listed Ernst, Frik and Ott,[6] Chaoul,[4] Morison, Hugo and Mayneord,[8] and more recently, Braestrup and Blatz[2] as having all published excellent monographs on the physics of short distance therapy. Bromley[3] has published a fine paper on the clinical aspects of contact therapy.

APPLICABILITY

With the unusually short target-skin distance there is a sharp drop in intensity within the first centimeter of tissue. The proportionately high surface intensity constitutes this as a method of roentgen cauterization.

The diameter of the tube head is small and except in special circumstances limits the size of the lesion to be treated to 2.4 cm. Larger lesions require multiple portals. Applicability of this type of therapy is therefore most suited to the following circumstances:

1. Pathological conditions at or near the surface with limited infiltration.
2. Lesions in the accessible body cavities, such as mouth, vagina, or rectum.
3. Tumors which can be exposed surgically, such as those in bladder or stomach.
4. The area should be of limited dimensions.

This method of therapy has the advantage of convenience, speed, and economy. For instance, a patient with a basal cell carcinoma may be adequately treated in

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from thirty to sixty seconds. The treatment of 100 patients, such as reported here, formerly constituted a large administrative as well as therapeutic problem. Previously, many of these patients required hospitalization for radium application or other reasons, as compared with most of the cases in the present series who were ambulatory and required no hospitalization. The monetary savings probably amounted to several thousand dollars in this series. Formerly, a hospital admission for radium application would cost the City of New York between fifty and sixty dollars, excluding the cost of the radium. Cost per treatment with the present therapy is estimated at less than one dollar. Its use in a large cancer hospital lifts a real burden from an already busy radiation therapy division and also liberates the operating room facilities for other surgical cases.

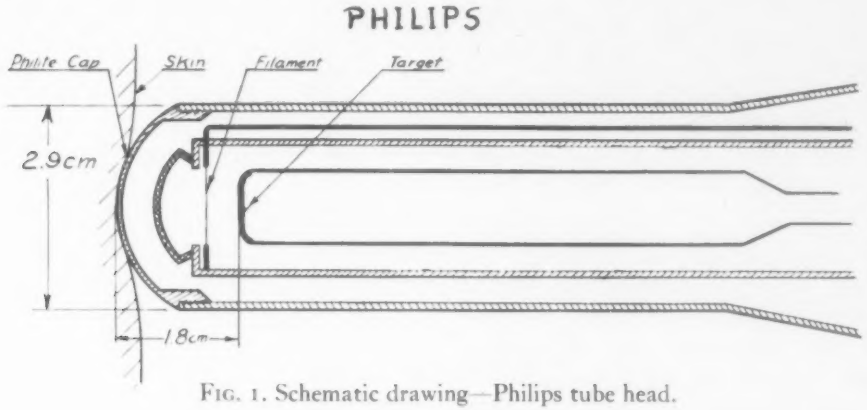

Fig. 1. Schematic drawing—Philips tube head.

Formerly inaccessible locations can now be treated conveniently because of the small size of the tube head, and its more accurate focus (Fig. 4). The small tube head allows more protection to neighboring vital structures than could hitherto be obtained. A lesion of the eyelid may be treated with no exposure to the structure of the eye lens. Similarly, lesions within cavities which have received the limit of external irradiation

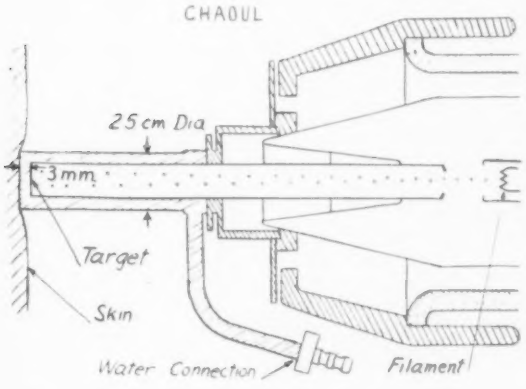

Fig. 2. Schematic drawing—Chaoul tube head.

Fig. 3. Contact roentgen radiation application.

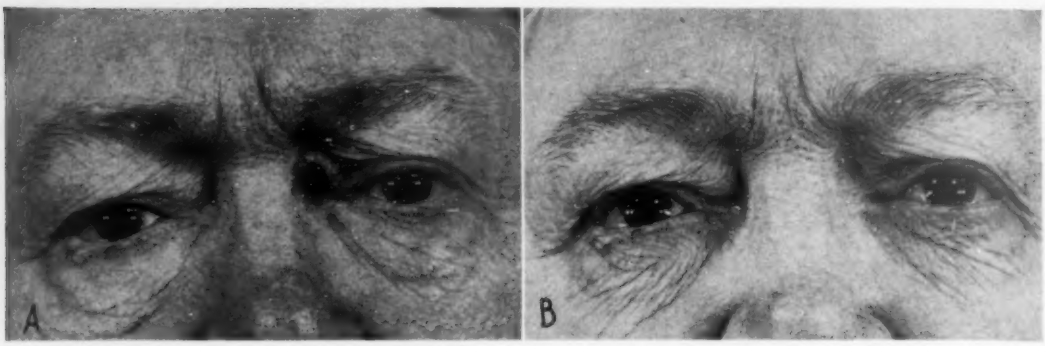

FIG. 4. Basal cell epithelioma of the inner canthus; difficult location for usual type of roentgen treatment. Patient W. M. *A*, before contact roentgen therapy, dosage of 13,000 r; *B*, three months after therapy.

may be given additional radiation therapy through this medium. Thus a patient with a cancer of the bladder which recurs after all the skin portals have been utilized to their full tolerance may be given additional roentgen therapy through a cystostomy opening.

Most of the rays are absorbed in the first few millimeters of tissue. A carefully graded roentgen therapy technique should maintain the viability of the tumor bed while eradicating the tumor. This is important in lesions which lie just over bone or cartilage.

Cosmetic results are good. Lesions which might formerly have required mutilating surgery, such as those about the eye, are now treated with this method with minimal scarring.

The method lends itself to the treatment of multiple small lesions which are often encountered and which previously offered a laborious therapeutic problem. Thus one case with eleven keratotic areas was treated in five and one-half minutes, thirty seconds being sufficient for the irradiation of each lesion.

In aged, infirm or psychiatric individuals, who cannot tolerate lengthy treatments or who would otherwise require hospitalization, this method finds a good use. Patients may be treated in a short time with no physical inconvenience.

This treatment can be combined with other procedures; for instance, used as a cautery to clear up superficial overgrowths, and later followed by treatment with more penetrating rays or surgery.

Patients with advanced cancer may have excellent psychological palliation by the method of treating one of the visible lesions and causing it to subside.

LIMITATIONS OF THE METHOD AND APPARATUS

(1) The method must be used strictly within the field of applicability; if not, the subsequent therapeutic procedure may become complicated.

(2) No adequate provisions are made for the protection of the operator. For the sake of mobility and convenience only a small lead glass disc is supplied to block stray radiation from the end of the tube. This cuts down considerable stray radiation but it is cumbersome and gives a false sense of security. Braestrup and Blatz have measured the stray radiation and have obtained the following figures, using no filter, no diaphragm and no lead disc:

(a) One meter from tube end—along cable—0.02 r per minute.
(b) At position of operator's hand if tube is held—0.08 r per minute.
(c) One meter from tube end in a direction 45° from the tube axis—0.03 r per minute.

(3) Dosage measurement may be inaccurate as the intensity of the output is

so great. Small doses are given accurately only with great difficulty; for instance, a dose of 400 r is given in less than two seconds, and even when timed with a stopwatch, the dose may be inaccurate.

(4) The filters and cones are held in place on the tube head by a crude home made arrangement of rubber bands. This has already been corrected in a later cone design.

DESCRIPTION OF APPARATUS

The short distance, low voltage therapy unit used in this report was designed by Philips. All the essential components except the tube are contained in a small movable cabinet. A shockproof cable connects the unipolar shockproof roentgen tube to the unit. The tube is cooled by means of forced air circulation. An automatic timer is built into the machine. As with the Chaoul unit the rays emerge axially from one end of the tube and permit a short target-skin distance. In the Chaoul apparatus there is a gold plated nickel target mounted at the extreme end which serves as both target and filter. The useful beam passes through the target; the target skin distance is unusually short, 3 mm. In the Philips tube the rays do not pass through the target. The target-skin distance is 1.8 cm. and the inherent filtration of the tube is only 0.2 mm. Al equivalent. Figures 1 and 2 show the two short distance, low voltage roentgen tubes for comparison. The Philips tube is contained in a metal cylinder which can be aimed in any direction by a dental type support consisting of a system of balanced hinges and knobs. When necessary it may be held in the hands during application. This should be discouraged to avoid unnecessary exposure to the radiologist. A number of metal cones with various sized openings may be placed over the tube head to limit the diameter of the field. Aluminum filters of 1.0 and 2.5 mm. Al are provided. These may be placed over the tip of the tube head. A protective lead glass disc may be used near the end of the tube which decreases the scattered radiation to the operator. The tube becomes top heavy when this lead glass disc is used and makes delicate localization difficult. These defects are minimal and can be easily corrected in future designs. Braestrup and Bierman[1] have recently devised a suction cone which when screwed to the tube furnishes a method for holding it in accurate alignment to the area being treated by gently sucking the exposed part toward the tip of the cone.

PHYSICAL FACTORS

In general, the apparatus offers a convenient means of approximating the dose distribution obtainable with radium, the dosage rate, however, being much higher. In the treatment of superficial lesions a very large dose can be given at the surface in a short time with relative protection of the underlying structures. When an increase in depth dose is desired, Braestrup and Blatz have shown that the first millimeter of aluminum filter improves the depth dose considerably, while any further increase in aluminum filtration gives but little gain. Table 1 shows the figures for the tube output at the last calibration and the percentage depth dose at 1 and 5 cm. The factors used are 45 kv. and 2 ma.

Braestrup and Blatz used Pendergrass' figures for the water-cooled Chaoul tube and compared its physical factors to that of the air cooled Philips tube under discussion. Due to its low inherent filtration, the Philips tube was found to have a dosage rate per milliampere which was twenty-five times that of the Chaoul type. If the filtration is equalized by adding 0.2 mm. Cu and 1 mm. Al to the Philips tube, then at equal distances the r per milliampere-minute is about the same. However, with equal voltages the radiation quality of the air cooled type has a half-value layer of 0.28 mm. Al, while the water cooled type has a half-value layer of 3.8 mm. Al. When the Chaoul tube is used in contact, the estimated dose at 1 cm. depth is approximately 5 per cent. The voltage rating of both types is between 45 and 60 kv., and is

the present maximum which contact tube construction will allow. One of us (W.E.H.) who uses the Chaoul type of tube in his private practice believes that with equal dosage the radiation effects are equivalent. Certainly the rationale and applicability of both types is very similar. This report, however, concerns itself with the first hundred consecutive cases treated at the Brooklyn Cancer Institute with the Philips type of tube.

TABLE I

MACHINE SETTING

		Voltmeter	Sphere Gap kv.	Milliamperes		
		On Line	45	2		
Filter Al mm.	Focal skin distance cm.	Time in minutes and seconds to deliver dose indicated			Roentgens per minute in air	Depth dose at 1 cm. (5 cm.)
		r 10,000	r 1,000	r		
0	1.8	0′48″	0′4.8″		12,600	per cent 23 (0.6)
	2.0	(1′22″)	(0′8.2″)		7,350	
	3.8	3′32″	0′21.3″		2,820	36 (1.7)
1.0	2.05	5′43″	0′34″		1,750	36 (1.9)
	4.05	22¼′	2′14″		449	51 (4.4)
2.5	2.05	14½′	1′27″		693	40 (3.0)
	4.05	56¼′	5′37″		178	57 (7.0)

DOSAGE

Except when otherwise indicated, all of the patients treated were exposed to roentgen rays generated at 45 kv., 2 ma., 1.8 cm. target-skin distance, no filter. The output of the machine is calibrated at least once per month and with different tubes was found to vary between 10,000 and 13,000 r per minute. Many of the patients with epithelioma were given single cauterizing doses to the surface of approximately 13,000 r, which were limited to lesions 2.45 cm. in diameter or smaller. Experience has taught us that this is probably close to the full tolerance of the tumor bed since there were some cases who developed chondritis, and others had delayed healing with skin atrophy. For surface cauterization we have therefore reduced this dose to 10,000 r. This is well above the lethal dose for the skin lesions encountered and permits good healing. This dose has been found to be entirely safe for all lesions except those lying on cartilage. To such sites, we give 5,000 to 6,000 r in one sitting and have had no difficulty with healing except where a

pre-existing chondritis was present. In these cases we have fractionated the dosage to give 500 to 1,000 r daily for a total of 5,000 to 6,000 r, the reaction being observed and the treatment modified, if indicated, as the case is treated.

Special precautions must be taken in the treatment of lesions occurring at the edge of previously treated areas. A smaller total or fractionated dosage is preferable here because of the danger of intractable breakdown of a radiation scar. For cornified, piled up lesions, which are on the surface, it is occasionally safe to go much higher than 10,000 r in one sitting provided the rays are absorbed in tumor tissue. In such cases, the only dosage estimate need be for the amount received in the underlying bed. We have given over 20,000 r with resultant good healing. Additional filtration may be used when an infiltrative character of a tumor is suspected. The addition of 1 or 2 mm. Al filter increases the target-skin distance to 2.05 cm. and reduces the output, as may be seen from the dosage chart. The optimum filter is 1 mm. Al since there is little improvement in depth dose with greater filtration. The therapy is usually fractionated when using a filter, giving from 500 to 1,000 r daily for totals varying between 6,000 and 10,000 r.

Areas measuring more than 2.45 cm., which is the size of the tube head, can be treated by crossfiring with fractionated technique or by increasing the target-skin distance and using the tube without a cone. The lesion is blocked off with lead foil or lead rubber and the rays permitted to spray its entire surface. No filter is used and from 6,000 to 10,000 r can be given. The edge of the lesion may receive somewhat less exposure because of the greater target-skin distance at the periphery.

Where only a small dosage is desired, one is forced to increase the target-skin distance or add a filter to decrease the intensity. The present output is 1,000 r in 4.8 seconds when used without filter at the tube surface. In order to give 500 r, the machine would have to be run for only 2.4 seconds. With the present timing device, this may result in inaccurate dosage. By increasing the target-skin distance 2 cm. or adding 1 mm. Al filter, this dose can be given more accurately.

The erythema dose for unfiltered rays at contact is estimated as 400 r.

Non-malignant lesions have of necessity been given smaller single and total doses. The technique is described under the individual headings in the latter part of the paper.

The therapeutic ingenuity of the roentgenologist, when utilized within the field of applicability of the apparatus, can give this method a wide range of usefulness.

HISTOPATHOLOGY

After the usual cauterization dose of 10,000 to 13,000 r there is often almost instantaneous edema which may last several hours. Histopathologically, this is reflected as an immediate vascular dilatation with a perivascular leukocytic response. By the end of twenty-four to forty-eight hours, the skin shows a well demarcated erythema which develops a deeply pigmented hue in from seven to fourteen days. During this period, the tumor cells show either swelling or shrinking of the cytoplasm. Cell boundaries are poorly defined. There are no mitotic figures. The nuclei become hyperchromatic and shrunken. Eventually only shadow forms are seen. The stroma about the groups of tumor cells increases in amount and becomes myxomatous in appearance. The walls of the swollen blood vessels are thickened and there is a scant perivascular lymphocytic infiltrate. Finally, the surface crusts over and regeneration with scar formation and some pigmentation takes place in from four to eight weeks. Histologic sections at this stage show some atrophy of the epidermis and increase of chromatophores and fibrous tissue in the corium.

POSITIONING THE PATIENT

The proper cone diameter is chosen by fitting various cones over the lesion and

TABLE II

TYPES OF CASES TREATED

Basal cell; skin; curable	44	
Basal cell; skin; palliative	7	
Rodent ulcer; skin; palliative	4	55
Squamous cell; skin; curable	7	
Squamous cell; elsewhere; curable	3	
Squamous cell; elsewhere; palliative	12	22
Adenocarcinoma; palliative; stomach	1	
Adenocarcinoma; palliative; colostomy overgrowth	1	
Adenocarcinoma; palliative; breast metastasis	7	9
Kaposi's hemorrhagic sarcoma		2
Keratosis		4
Verruca		3
Corn		1
Acne keloid		1
Angioma		2
Furunculosis		1
		100

observing it through the opening which ordinarily fits over the tube cap. In epithelioma an area of normal skin from 0.3 to 0.5 cm. is included around the circumference of the lesion. Some of the cones have smaller diameter tips added which increase the target-skin distance by another 2.0 cm. These small tips may be used in the approach of otherwise inaccessible areas into which the whole tube diameter will not fit. Other tips leave the tube face at an angle and permit the turning of the cone in such a direction as to irradiate a lesion and furnish protection to vital structures.

TABLE III

LOCATION

	Cases	
Skin (head)		
Face	23	
Ear	3	
Nose	22	
Lid	2	
Canthus	9	
Cheek	6	65
Skin (elsewhere)		11
Bladder	1	
Buccal mucosa	1	
Breast metastases	7	
Lip—upper	2	
lower	3	5
Stomach	1	
Submental metastasis	1	
Floor of mouth	4	
Colostomy opening	1	
Scrotum	1	
Palate	1	
Axilla	1	24
		100

TABLE IV

RESULTS—BASAL CELL CARCINOMA

Basal cell carcinoma	55 cases
Considered curable when first seen; biopsy proved	42
Cases which received previous therapy	12
Cases which required re-treatment	7
Controlled cases	41
Poor results, although controlled	1
Complications:	
Delayed healing due to chondritis	5
Delayed healing due to treatment past tolerance	1
Required manipulative dilatation of lacrimal duct	3
Slight bleeding from nose during reactive period	19
Loss of few eyelashes	1
Conjunctivitis (transient)	1
Palliative (basal cell)—(7 cases)	
Previous treatments	5
Required secondary treatment	2
Controlled	3
Well palliated	2
Poor result	2
Complications:	
Punched-out area, unhealed, past tolerance	2
Palliative (basal cell—rodent ulcer)—(4 cases)	
Previous therapy	4
Required multiple treatment	4
Lesion appears controlled	3
Lesion made progress despite treatment	1
No biopsy (1 case)	
Controlled	1
Necrotic tissue (1 case) clinically basal cell	
Controlled	1

The patient is seated in good light, preferably in such a position that the part to be treated is immobilized. A dental chair is excellent. In any case, the part to be treated should rest on some stable object.

Great care should be exercised in the localization of the lesion. The setting of the tube in contact with the area to be treated may be done in various ways:

(1) By direct visualization.

(2) Another excellent method is to start the cooling system. This automatically lights the tube filament and the thin bakelite tube cap glows with sufficient intensity to dimly illuminate the field. This is best used when the room is darkened and cannot be used when a filter covers the tip. One of us (M. R. C.) is at present developing a luminating device. It consists of a transparent or translucent material such as lucite, which can be used to seal the end of the tube. Sufficient light will come through when the filament is lighted to illuminate the field. Transparent filters of aluminum equivalent would also allow the filament light to come through.

(3) With the cone held in place over the lesion a line is drawn on the skin in ink around the circumference of the cone. When replaced within the drawn circle, the cone automatically fits over the lesion.

(4) On occasion the cone is held in position over the lesion and the tube pushed into it. This method requires an assistant.

(5) In cavities the tube is occasionally set by palpation.

REVIEW OF FIRST 100 CASES TREATED AT BROOKLYN CANCER INSTITUTE

Fifty-five cases of basal cell carcinoma were treated (Table IV). These were located in the skin in various places about the head and face. All diagnoses were confirmed by biopsy, except two.

In estimating final results, it is important to divide all of the 55 basal cell lesions into prognostic groups. Forty-four were judged to be curable when first seen, although 12 of these had had previous therapy of various types and amounts, including surgery. Seven were so extensive as to be judged palliative problems and an additional 4 were such extensive rodent ulcers that but a small amount of improvement could be expected.

Basal Cell Carcinomas Judged Curable. Of the 44 cases judged curable, 100 per cent were controlled. Secondary treatment was required for residual nodulation to one side of the area treated in 8 of the 44, or 18 per cent. The most common cause for this additional treatment was slight movement of the patient, or tube head, away from the original setting. In a rare case, the lesion may have extended beyond the diameter of the cone cap. Although 100 per cent of the cases were controlled, it is only six months since the last case of this series was treated and others may certainly report back with recurrences. There were 6 cases with delayed healing, 3 of which had a second cauterizing contact dose. Five of these cases were judged as delayed, because of chondritis which developed in underlying cartilage (Fig. 5, 6 and 7). Four of 19 nasal lesions which fell into the curable group and 1 of the 3 involving the ear lobe had this complication. There are four principal factors responsible for this sequel:

(1) Chondritis was present in most of these cases before therapy was instituted.

(2) Cartilage is notorious for its poor toleration of radiation.

(3) Overtreatment must be considered as a factor.

(4) Secondary infection of the irradiated tissue is an additional cause.

Because of these results, dosage in the treatment of lesions which lie on cartilage has been reduced or changed to a fractionated method. In this group, healing is not complete in the one case which was judged to have poor final result. This took place in an extremely uncooperative patient who refused to attend the clinic because he was not bothered by the small residual crusting. Other complications seen in this group were considered minor and included slight tearing of the eyes from fibrosis of the lacrimal ducts in 3 cases, which required subsequent probing and dilatation. This complication cannot be blamed entirely on the therapy, since the lesions themselves were undoubtedly a contributory factor. Of secondary importance was the loss of eyelashes in the eyelid and some nasal congestion with bleeding in all of the nasal cases.

Basal Cell Carcinomas Judged Palliative Problems. There were 7 cases of basal cell carcinoma which because of their size, location, or extent of previous therapy were judged to be palliative problems only. Three cases were ar-

FIG. 5. Basal cell epithelioma over cartilage—chondritis. Patient N. F. *A*, before contact roentgen therapy, dosage of 13,000 r, one treatment; *B*, end-result from loss of cartilage five months after therapy.

FIG. 6. Basal cell epithelioma over cartilage—chondritis. Patient A. R. *A*, before contact roentgen therapy, dosage of 13,000 r, one treatment; *B*, ten months after therapy.

FIG. 7. Basal cell epithelioma over cartilage—chondritis. Patient W. K. *A*, before contact roentgen therapy, dosage of 13,000 r, one treatment; *B*, eleven months after therapy.

rested, an additional 2 were palliated and poor results were obtained in two. Of those that were arrested, 1 case responded surprisingly well to a single dose of radiation to each of two large lesions, one on the forehead and one on the temple, each measuring 3.5 by 1.5 cm. in size (Fig. 8). The longest diameter of the lesions in this case was greater than the diameter of the

tube head. The lesions were therefore blocked with lead and the cone removed to a target-skin distance of 3.8 cm. In this way the rays were allowed to spray the entire lesion. The forehead was given 11,800 r, using no filtration and the temple was given 8,880 r. The lesions

Fig. 8. Basal cell epithelioma. Diameter of lesions larger than tube head. Patient M. C. *A*, before contact roentgen therapy, one treatment, 11,000 r, target-skin distance 3.8 cm.; *B*, five months after therapy.

flattened out after a considerable reaction and left a slightly atrophic pliable scar (Fig. 8, *B*). No recurrence was present one year after therapy.

Another case had an extensive basal cell carcinoma of long duration, superadded to a lupus vulgaris of many years' standing, which had proved to be most intractable to various types of therapy (Fig. 9). Seven areas were blocked with lead rubber and single treatments of 13,000 r each delivered. First the extension to the lip was treated; three weeks later the right side of the nose; nine weeks later the upper lid and side of the nose; eight months later three separate residual lesions. Treatment was given cautiously and at long intervals of time because of the great danger of necrosis and non-healing. The lesion improved remarkably as may be seen in the accompanying photograph (Fig. 9, *B*).

One case exemplified the possible use of the contact roentgen machine in combination with

FIG. 9. Basal cell epithelioma superposed on a lupus vulgaris. Patient M. B. *A*, before contact roentgen treatment with multiple portals, 13,000 r each; *B*, ten months after therapy.

other types of radiation therapy. A patient appeared who had a large infected basal cell carcinoma on the face in the area draining into the cavernous sinus. Squamous elements were present histologically. There was considerable swelling and induration around the base and the lesion was considered too large for contact roentgen therapy (Fig. 10). The whole area was therefore blocked with lead rubber and exposed to the following radiation: 130 kv., 30 cm. target-skin distance, 3 mm. Al filter, 200 r given daily for a total of 1,200 r. No further therapy was given at this time because of the grossly infected appearance of the contiguous skin which lay in the drainage area of the cavernous sinus. Following this, the lesion became smaller, well demarcated and the inflammation subsided (Fig. 10, *B*). Unfortunately through mis-

FIG. 10. Basal cell carcinoma plus infection. Patient D. C. *A*, before treatment with combination of low voltage and contact roentgen therapy; *B*, five months after therapy.

understanding, the patient supposed that his treatments were completed and therefore did not report back to the clinic. At the end of three months, he returned with considerable residual carcinoma. This was then crossfired with fractionated doses of contact therapy, an additional filter of 1 mm. Al was added; 1,000 r was given to each of two portals for six consecutive days. The eye and nose were protected with lead rubber. The lesion reacted favorably and no recurrence has been noted in six months.

Of the patients who received palliation, one had a lesion at the outer canthus of the eye invading the orbit. This was treated with plastic surgery and a small recurrence at the edge of the wound eradicated with fractional treatments. A special eyelid cone was used which increased the target-skin distance to 4.05 cm., and 1 mm. Al filter was added; 500 r was given on each of nine subsequent days. The lesion has since recurred at the original site, but the area treated with contact roentgen therapy appears to have been sterilized.

Two cases might be said to have had poor results due to the therapy received. Both were left with small, punched out, unhealed ulcers. The first case had a recurrence at one edge of a thinned out, atrophied scar. He had previously had various and extensive radiation exposures over a period of years. He was given 13,000 r to one small nodule in the edge of this scar. The reaction did not result in healing and he was given another similar exposure six months later. A necrotic, punched out, non-healing ulcer resulted which has not regenerated in eight months. The area treated, however, shows no evidence of residual epitheliomata.

A similar poor result was obtained in another instance where the patient had previously received extensive therapy to a basal cell carcinoma arising in an old scar of the skin over the Achilles tendon. After the patient refused amputation, he was given 13,000 r of unfiltered radiation in one sitting as a trial. The ulcer, though still present for over a year, is healing slowly and the patient has not had to submit to an amputation.

Fig. 11. Squamous cell epithelioma. Patient R. D. *A*, before therapy with contact fractionated crossfire technique; *B*, two and one-half months after therapy.

Recurrences in lesions which have received extensive therapy, which are accompanied by unhealthy scarring and other late effects of radiation, are better treated by surgery.

Rodent Ulcers. Of the 55 basal cell carcinomas treated, 4 were rodent ulcers. Three of these were well palliated and one died. The first patient had had a slowly extending rodent ulcer since 1918, which had destroyed the entire anterior maxillary antral wall and extended into the antrum. Multiple areas were chosen and the treatment cone was placed directly into the cavity of the exposed antrum, in contact with the extensions. Other types of therapy might have resulted in exposure to the eye. The patient has been treated on four different occasions, each time eradicating the lesion in the area treated. In another of these unfortunate cases the whole nose was eaten away. The ad-

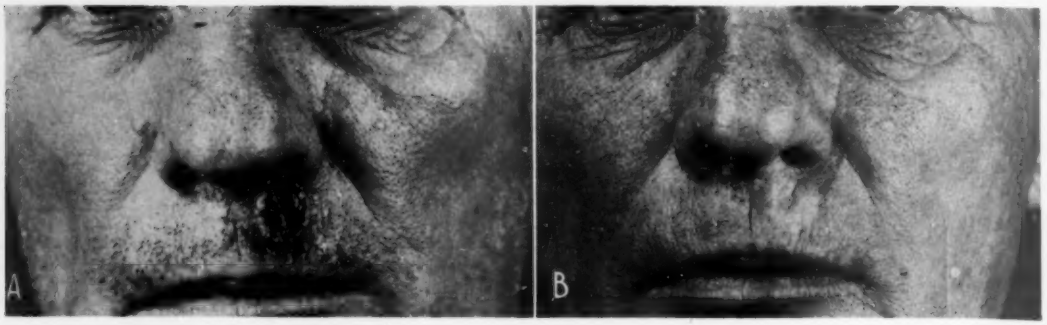

Fig. 12. Squamous cell epithelioma. Patient S. V. *A*, before treatment with contact roentgen therapy, dosage of 21,800 r, one treatment, to compensate for increased depth of lesion; *B*, three months after therapy.

vancing edges of the lesion were treated and its progress appears to have been delayed.

The patient who died had the whole side of the cheek eaten out, with the ramus of the mandible destroyed and the advancing carcinoma extending into the buccal mucosa, floor of the mouth and tongue. Contact roentgen therapy was utilized for psychic reasons to bolster the morale of the patient.

Squamous Cell Carcinoma of Skin Judged Curable. There were 7 cases of squamous cell carcinoma of the skin which were judged curable when first seen. The majority were treated as were the small basal cell lesions, with from 10,000 to 13,000 r, unfiltered contact roentgen therapy at a single treatment; only 1 of these required a second treatment. All were controlled. In 2 cases, because of the large size of the lesion, fractionated therapy was prescribed. Similarly a 1 mm. Al filter was utilized in 2 cases because of the deeper infiltrative character of the tumor. When the lesion is of greater diameter than the treatment cone and of irregular circumference, fractionated therapy, using the crossfire technique, is the method of choice. For example, the first patient so treated had a cauliflower overgrowth in the left cheek beneath the eye (Fig. 11). She was given four treatments, using 1 mm. Al filter, 2.05 cm. target-skin distance, 1,000 r to each of two portals, crossfiring the lesion for a total of 4,000 r to each. Twenty days after the last treatment the lesion had flattened out even with the skin surface. One month after therapy, the result could be estimated and an additional single dose of 12,000 r unfiltered radiation was

Fig. 13. Squamous cell epithelioma. Patient M. C. *A*, before contact roentgen therapy, fractionated technique; *B*, four months after therapy.

given to a residual nodulation in the upper angle of the lesion (Fig. 11, *B*). When last seen, one year later, no residual cancer could be detected.

When the cancer was superficial, but piled upon the surface to a greater thickness than usual, a large cauterizing dose was given with no filtration, so that the underlying tumor bed could be spared. One patient who had a squamous cell carcinoma of the skin beneath the nose is illustrated in Figure 12.

In another instance, a squamous cell carcinoma of the cheek was treated with the fractionated technique, delivering 1,000 r at contact daily for ten treatments, using 1 mm. Al filter (Fig. 13). Five days after the last treatment an exudative reaction could be seen. Crusting was removed periodically to free the retained secretion. Seven weeks after the therapy, the lesion was judged healed (Fig. 13, *B*).

Fig. 14. Recurrent squamous cell epithelioma of lower lip. Patient B. P. *A*, before treatment with contact cauterization. First treatment, 39,000 r. Eight weeks later 13,200 r followed later by 6,500 r; *B*, fifteen months after therapy. This intense dosage is to be used only under unusual circumstances; see text.

Squamous Cell Carcinoma of Lower Lip. There were 3 cases of squamous cell carcinoma of the lower lip. All were treated successfully. Since almost certain eradication may be obtained by more tried methods, we did not feel free to treat many patients with this method.

The special circumstances for the utilization of contact roentgen therapy are as follows: very superficial lesions, or recurrences which have previously received extensive therapy and where surgery has been refused. Of the 3 patients treated, 1 had an overgrowth on one side of the lip treated by excision, biopsy of a superficial scabbing area on another part of the lip was reported as squamous cell carcinoma and treated by a single dose of unfiltered contact therapy of 13,200 r. The reaction subsided within six weeks and nine months later the lip was free of any demonstrable pathological lesion.

Another more complicated case had a recurrence on the lower lip, following roentgen therapy elsewhere. He refused surgery and was given a large single dose of 39,000 r because of the infiltrating character of the lesion (Fig. 14). The reaction subsided in about eight weeks with some residual scabbing, to which an additional 13,200 r was given. A small ulcer formed at the site of exposure which upon biopsy study was reported as chronic inflammatory tissue with ulceration. But suspicion of malignancy persisted clinically, and the patient was then given a further treatment with 6,500 r. When last seen, the patient showed a well healed scar with no evidence of induration. In justification of this cauterizing dosage, Van der Plaats has stated that a surface dose of even 47,000 r is of no particular significance when the surface consists of tumor tissue for which no lethal maximal dose exists.

Squamous Cell Carcinoma, Palliative. Twelve cases of advanced or intractable squamous cell carcinoma were treated for palliative or psychotherapeutic reasons. While we do not feel that the small penetration of this type of radiation is most appropriate for the infiltrative character of these squamous cell lesions, nevertheless it is sometimes applicable for palliation in exposed lesions. In this group are 4 advanced

FIG. 15. Kaposi's disease. Patient A. P. *A*, before contact roentgen therapy; *B*, two months after therapy; pigmentation still present (forehead).

lesions of the floor of the mouth, 2 in the submental region, 1 on the palate, cheek, nose, skin elsewhere, scrotum, and finally 1 within the bladder extending from a cervical carcinoma. In this last case, the skin portals had been previously utilized to their full tolerance. The contact therapy tube was applied through a cystostomy opening at 4.05 cm. target-skin distance, 1 mm. Al filter, 10,000 r delivered in twenty and one-half minutes. Lesions in most of these cases were diminished in size with exuberant overgrowths flattened down and troublesome discharge and odor lessened.

Adenocarcinoma, Palliative. Except under special circumstances, it is improbable that this method of therapy will supplant older methods in the treatment of adenocarcinoma. In order to reach the lesion, the adenocarcinoma must be located near a body orifice, as in the terminal rectum, be exposed surgically, or its metastases appear on a body surface. In any case, this type of treatment can be used in such cases as a palliative procedure only. In this series, 1 primary and 8 metastatic adenocarcinomas were treated. An extensive carcinoma of the stomach was found during an exploratory laparotomy

FIG. 16. Kaposi's disease. Patient A. P. *A*, showing lesions on hands before contact roentgen therapy; *B*, fourteen months after therapy. Individual lesions treated at different intervals with varying doses.

and irradiated through the stomach wall via three areas using 1 mm. Al, 2.05 cm. target-skin distance, for a total of 1,890 r to each area. The effect of this irradiation could not be studied as the patient died ten days later of pulmonary edema.

This method of therapy is applicable in the treatment of inoperable cancer of the stomach only when a gastrostomy of sufficient diameter is made to permit the entrance of the tube head directly into the stomach to allow contact with the lesion. Another patient had a neoplastic overgrowth about a colostomy opening treated. The local area reacted favorably with a decrease in size and diminution in troublesome discharge. Seven patients were treated who had skin metastases or extensions about the scar from carcinoma of the breast. The local lesion was destroyed in practically every case. One patient had multiple subepidermal nodules scattered over the skin of the entire body. These were treated as they appeared. A single treatment of 6,500 r delivered to the skin was sufficient to control each metastasis.

Keratoses. Contact roentgen therapy may be used as a prophylactic. This is well demonstrated in the prompt destruction of premalignant senile keratosis. A dosage of 3,000 to 6,000 r at one sitting has been found sufficient to eradicate these lesions.

Multiple Idiopathic Hemorrhagic Sarcoma (Kaposi's Disease). Two patients were treated. In each case lesions were small, discrete, on the surface and were well adapted to this type of therapy. The first patient had a single lesion on the thigh which was given 13,000 r. When seen one year later, only a small depressed scar remained. Another patient had numerous discrete lesions scattered about the skin of the face and extremities. These lesions were treated with varying factors. One received 13,000 r without filter. Another was given 6,600 r with 1 mm. Al filter added. Another was treated with 3,420 r with 2 mm. Al filter. All the lesions subsided with little difference in the appearance of the pale atrophic scars. Since the lesion is superficially located on the skin, the most rational method would therefore be to use no filter and the shortest target-skin distance. From this experience we deem a dose of 6,000 r adequate. When this disease assumes a more diffuse form and is found in extensive plaques or ulcerations, this type of therapy would not be applicable (Fig. 15 and 16).

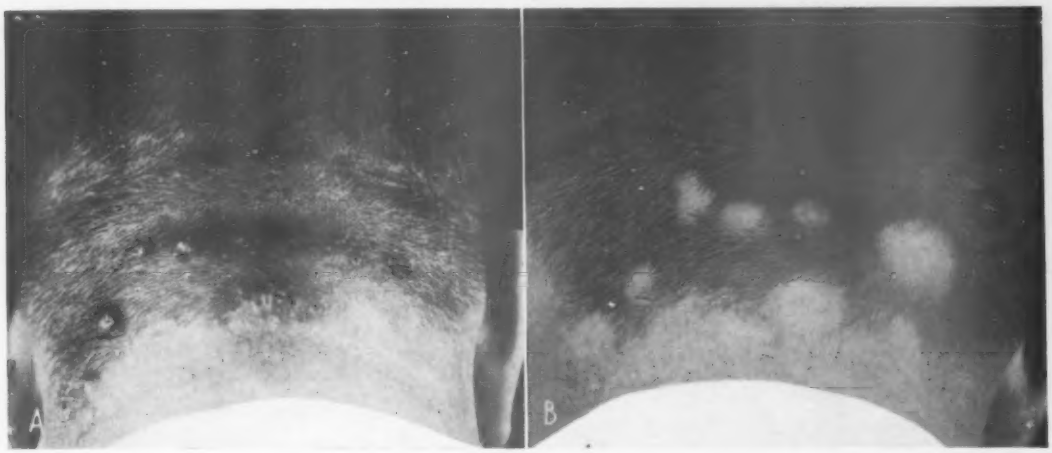

Fig. 17. Acne keloid. Patient R. M. *A*, before contact roentgen therapy; 6,000 r delivered to each lesion; *B*, eight months after therapy.

Verrucae and Corns. A patient with an extremely painful and disabling plantar wart was prepared by soaking of the foot and paring away of the top portion of the callus; 3,000 r at contact was given, and overnight the patient experienced relief of pain. The resulting reaction subsided in less than four weeks, with an excellent end-result. Another patient who had two warts on the sole of his foot was treated without preliminary soaking and paring of the warts. Each was given 6,600 r. He was not followed through the reaction but one year later there was no complaint.

A papillary growth present on a patient's nose

for one year so resembled a basal cell carcinoma that it was given a total of 13,000 r before the pathologist reported the biopsy as verruca. The reaction healed in four weeks leaving a pink smooth scar.

Furunculosis and Acne Keloid. A case of axillary furunculosis was treated. The contact tube was focused on each of several pustules. The result here was unsatisfactory because the disease was widespread. The process was later controlled by several treatments which included the entire axilla using a superficial type of roentgen therapy.

Where a follicular type of infection appears localized, however, a good result may be obtained. One patient had an intractable acne keloid which had been treated by various methods including roentgen therapy over a period of nine years (Fig. 17). Eight separate areas were chosen and cauterized with contact roentgen therapy, 6,000 r being given. A pale, epilated scar resulted at the site of each treatment and the disease was eradicated for the first time (Fig. 17, *B*). Ten months later no new lesions could be found.

Hemangioma. Two cases of hemangioma were treated during the period analyzed. The results were inconclusive in these 2 cases but our experience since that time has been most encouraging. An exposure of 600 to 1,000 r, without filter, produces visible changes. Additional therapy can be added as needed. Hemangiomas of the cavernous type should be treated with addition of 1 mm. Al filter.

SUMMARY

(1) The applicability, advantages, and limitation of contact roentgen therapy are listed.

(2) Dosage and technique as used at the Brooklyn Cancer Institute are described.

(3) The results of the first one hundred cases treated at the Brooklyn Cancer Institute are analyzed. Emphasis is placed on dosage and complications.

(4) The contact method of roentgen treatment is of distinct advantage in treating superficial lesions.*

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* For discussion see page 385.

Vol. 48, No. 3

THE LAYER TECHNIQUE IN RADIUM NEEDLE THERAPY*

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IN EACH center where interstitial radiation therapy is carried out, the clinicians have developed efficient techniques based to a large extent on experience. Reliable physical data for implanted sources of radiation are available but many difficulties are encountered when one attempts to evolve a simple method of dosage calculation.

In 1931 Martin, Quimby and Pack[6] described a relatively simple plan based on the observation that "*A spherical mass is equally well irradiated by a given quantity of radon whether concentrated at its center or subdivided and distributed geometrically about the center, provided that the implants are confined within the inner half of the radius.*" The dosage for a given tumor was designated as that amount sufficient to properly irradiate a sphere having a diameter equal to the greatest diameter of the tumor. In some instances, particularly where the tumors had irregular shapes, several such theoretical spheres large enough to enclose adjoining portions of the diseased tissue were used instead of a single large sphere. When such spheres had been laid out the proper amount of interstitial radon needed to produce a minimum of any given number of threshold erythema doses in each sphere could be quickly determined from a table. Although this method works quite well with rounded tumors, the values obtained are likely to be too high in flat or irregularly shaped neoplasms unless a very large number of spheres is used. In 1935 Quimby[8] described a simpler method derived from a great mass of experimental data. Tables were included from which the proper number of milligram- or millicurie-hours needed to produce a given minimum tissue dose in a tumor having a known volume could be easily obtained. The data were based on the assumption that all needles would be left in place four or more days, be evenly distributed and have a filter of 0.3 to 0.5 mm. of platinum. Laurence[2] also attempted to simplify the problem somewhat by calculating the dosage in roentgens at known points about standard radium needles and preparing charts and curves from which the dosage produced by various needle patterns could be ascertained.

In 1938 Paterson and Parker[7] published graphs from which the dosage in milligram-hours needed to produce a minimum of 1,000 gamma roentgens in a slab of tissue 1.0 cm. thick could be obtained when radium needles were placed in a plane in the center of the slab. Data were also included for needles placed in two or more planes at various distances from one another, and a formula was worked out for the minimum dosage needed to produce the same effect in various volumes of tissue.

The beginner in radiation therapy is often confused by the large number of variable factors involved in the determination of the tissue dose. In an effort to reduce the variables to a minimum a chart[4] prepared with the aid of Quimby was published in 1940 for three sizes of radium needles having a fixed amount of radium per unit of active length (0.6 mg.), a fixed filtration (0.5 mm. platinum), and a fixed treatment time (168 hours). The figures of the chart gave the threshold erythema doses at various points around each needle and from it the dosage at designated points in the tissue could be calculated for each needle pattern. With such an arrangement the pattern constitutes the only variable factor at the time of implantation. Since radium needles can be placed with more precision than the smaller radon seeds they are preferable for this type of work.

* Presented at the Twenty-sixth Annual Meeting, American Radium Society, Cleveland, Ohio, June 2–3, 1941.

The figures on the original chart covered only a few points around each needle and a new chart (Fig. 1) has been prepared with values indicated at millimeter intervals located from 0.3 to 1.5 cm. from each needle. The figures represent threshold erythema doses as calculated by Quimby over the center of each short needle, over the center and end of the active portion of each long needle, and over a point located three-fourths of the distance from the center to the end of the active portion of each long needle. The smallest needle contains 0.66 mg. in 0.5 cm. of active length but in the others the radium is distributed so that 1.0 cm. of active length contains approximately 0.6 mg. This type of loading was adopted because of Cade's[1] observation that "experience has shown that in the majority of cases of squamous celled carcinoma of the mouth, tongue and skin, 0.66 mg. of radium filtered with a minimum of 0.5 mm. of platinum produces cessation of growth in 1.0 cc. of tumor if left in place 168 hours." Reference to the upper drawing in Figure 2 indicates that a 0.66 mg. needle placed in the center of a cube measuring

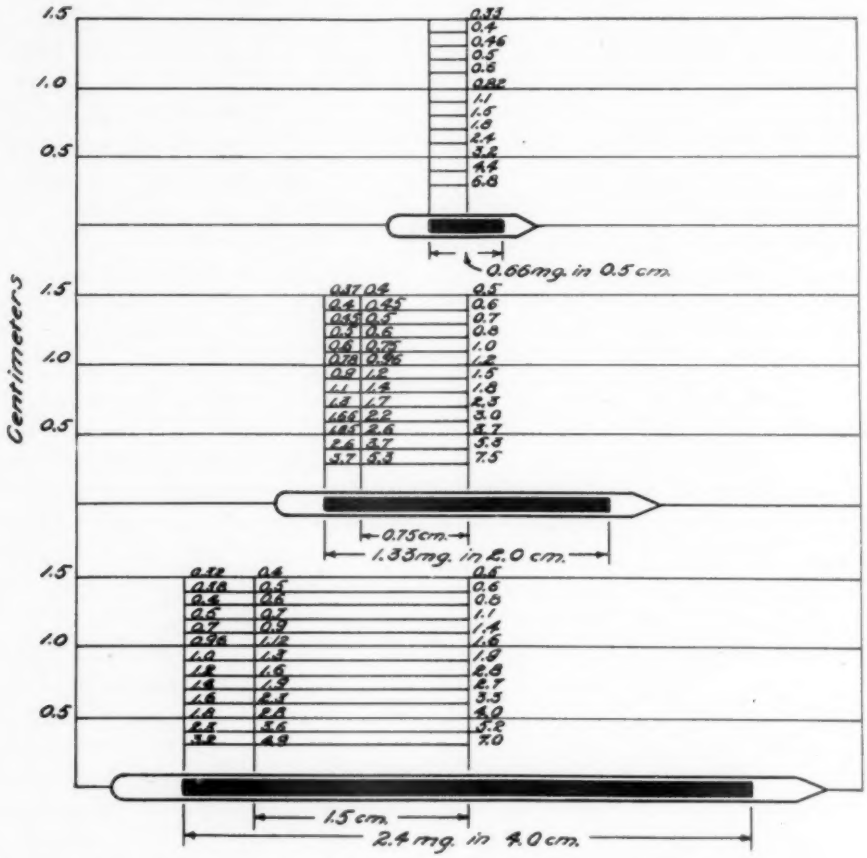
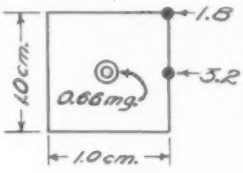


FIG. 1. Calibration chart showing the threshold erythema dose at points located 1.0 mm. apart about three types of low intensity radium needles when they are left in the tissues for 168 hours.

1.0 cm. on a side produces only 3.2 T.E.D. at the nearest point on the periphery and certainly such a dose could not be considered curative. However, the combination of the weak loading and the resultant longer time of application appears to reduce the reactions in the soft tissues to a minimum, and the needles have proved very satisfactory in practice. From the lower drawing in Figure 2 it can be seen that the 0.66 mg. needles may be combined so as to produce

efficient dosage in thin layers of tumor tissue and the long needles also lend themselves well to layer radiation.

In previous papers I have contended that with the factors given above a layer of squamous cell carcinoma 1.0 cm. thick could be cured by a series of the longer needles placed 1.0 cm. apart and parallel to one another so that the active portions extended beyond the borders of the growth. When the dosage at the outer corner of such a slab was estimated from the table in Figure 1, it was found to fall well below the 7 to 8 T.E.D. generally conceded to destroy squamous cell carcinoma. A careful



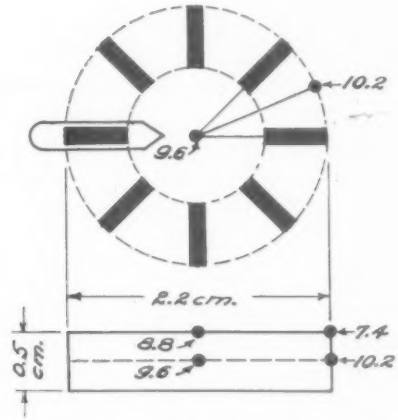


Fig. 2. The upper sketch represents the threshold erythema dose at points on the periphery of a cube measuring 1.0 cm. on a side with 0.66 mg. radium needle placed at its center for 168 hours. The lower sketch shows threshold erythema dose at points in a disc of tissue with eight 0.66 mg. radium needles planted radially in its central plane for 168 hours.

rechecking of successful implantations revealed the fact that the needles were really inserted from 0.7 to 0.8 cm. apart, and Cade has recently recommended this type of spacing.

The diagram shown in Figure 3 represents an implantation carried out for a squamous cell carcinoma of the lip having a surface area measuring 3.0 by 1.5 cm. The needles each contain 1.33 mg. of radium and are spaced 0.75 cm. apart. The figures represent the threshold erythema

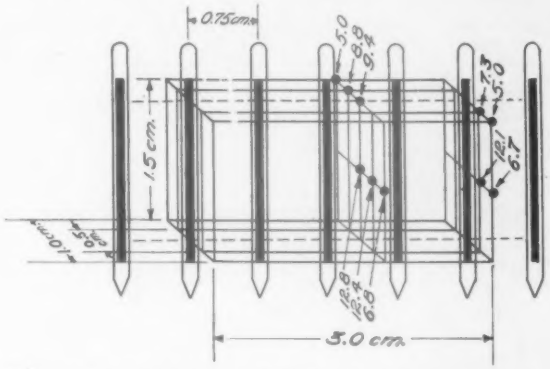


Fig. 3. Sketch showing threshold erythema dose at various points in slabs of tissue 0.5 and 1.0 cm. thick with 1.33 mg. radium needles planted in the central plane, 0.75 cm. apart, for 168 hours.

dose at the points marked by large black dots. It is interesting to note that the outer edges of the layer measuring 1.0 cm. in thickness receive only 5.0 T.E.D., whereas no portion of the layer measuring 0.5 cm. in thickness receives less than 7.3 T.E.D. These figures indicate that the layer of tissue efficiently irradiated measures only 0.5 cm. in thickness.

Some of the treated cases were reviewed in an effort to explain the good clinical results obtained by single layer implantations and it was noted that a large number of the lesions occurring on the mucous membrane of the soft palate, inside the cheek, floor of the mouth, tongue, lip and face measure little more than 0.5 cm. in thickness. The observation was also made that the needles were always planted in the base of the tumor, and it seems reasonable to assume that the destruction of the malignant cells in this region together with their blood supply should destroy the entire growth. When large proliferating tumors were treated the projecting portions were almost always removed with a high frequency loop before the implantation

was carried out. This procedure not only stopped all bleeding and provided material for microscopic study, but reduced the tumor to a flat slab measuring little more than 0.5 cm. in thickness. When the layer of tumor tissue was rounded and of moderate size a cartwheel pattern of 0.66 mg. needles of the type shown in Figure 2 was used with the outer ends of the needles

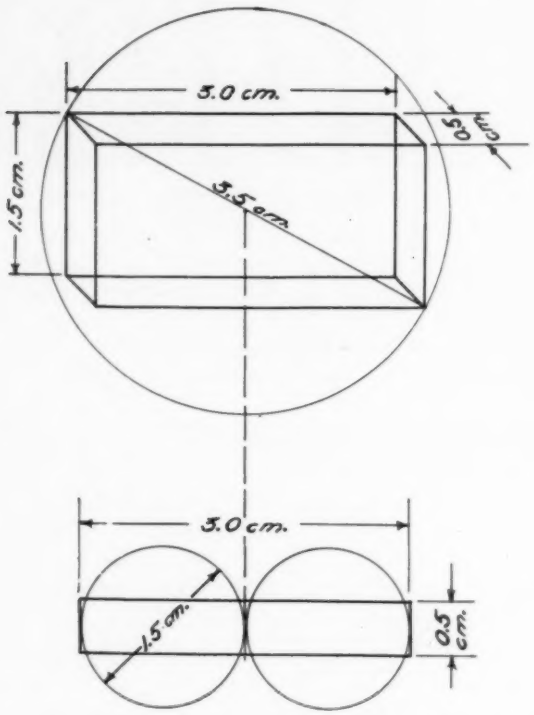


FIG. 4. Sketches showing that the dose for a slab of tissue measuring 3.0 by 1.5 by 0.5 cm. cannot be accurately calculated on the basis of one or two theoretical spheres.

spaced not more than 0.8 cm. apart. Calculations made from the dosage chart indicate that the extreme edges of a disc so treated received 7.4 T.E.D. This method was found particularly effective in the treatment of lesions involving the mucosa of the cheek and forming a saddle-like growth over the alveolus. Most radiation therapists employ contact applications for such tumors but the small needles can be stitched into the edges of the normal mucous membrane so that they will remain in place and assure a proper dosage in the base of the growth.

The sphere method of dosage calculation originally proposed by Martin, Quimby and Pack does not lend itself well to the estimation of the amount of radiation needed for thin layers of tissue. The upper drawing in Figure 4 shows that a single sphere with a diameter equal to the greatest diameter of a slab of tissue measuring 3.0 by 1.5 by 0.5 cm. has a volume far in excess of the involved region. The lower drawing indicates that doses based on the volumes of two smaller spheres each having a diameter equal to half the length of the slab are still too large to provide proper dosage for the tissue to be treated.

The volume of the layer of tissue under consideration is 2.25 cc. The proper dosage to produce a minimum of 7.0 T.E.D. in this amount of tumor is given as 608 mg-hr. or 4.5 millicuries-destroyed in Quimby's tables.[9] Some difficulty will be experienced in placing five 1.0 mc. radon seeds so that they will evenly irradiate the large area involved. Although the seven needles used in Figure 2 deliver 1,564 mg-hr. it must be remembered that the effect is distributed well outside the involved slab. If this dose were delivered with implants placed within the slab, the dosage at the center would be excessive. However, a layer of tissue of almost any size or shape can be treated by the addition of more evenly spaced needles without increasing the central effect appreciably, and it seems desirable to extend the zone of irradiation well beyond the palpable borders of the tumor in most instances.

A rounded tumor which cannot be reduced to a thin layer by electrosurgery may be treated by assuming that it is made up of several theoretical slabs of tissue, each of which is needled as indicated in Figure 2. Since the central effect is accentuated by adding extra layers of needles it has been found advisable to space them 1.0 cm. apart when two layers are used, and 1.5 cm. apart when three layers are used. In certain instances, particularly in the treatment of metastatic lymph nodes, doses larger than those delivered by the layers

Fig. 5. Appearance of large, flat, squamous cell carcinoma of face at the time of treatment, and six weeks and one year after treatment, with a single layer of low intensity radium needles left in place for 168 hours.

of needles just described have been deemed necessary. A method of safely providing this extra irradiation effect with divided doses of deep roentgen rays given over the needled area has been described in previous papers.[3,5]

The following case histories illustrate the layer method:

Case 1. (Fig. 5) J. T., male, laborer, aged forty-seven, applied for treatment because of an ulcer measuring 4.5 cm. in diameter, situated in the skin of the right temple just anterior to the ear. It had grown slowly for about two years and its growth had been much accelerated by the application of a caustic paste nine months prior to admission. The edges of the ulcer were thickened, with overhanging edges which measured about 0.5 cm. in thickness. Definite induration was felt outside these edges, particularly at the upper and lower border. The histopathological diagnosis made from a piece of tissue removed at the edge of the ulcer was squamous cell carcinoma, Grade 2. No metastatic lymph nodes could be palpated.

Treatment was administered by implanting six 2.4 mg. radium needles parallel to each other 0.8 cm. apart under the ulcer and ten 1.33 mg. needles with similar spacing under the induration above and below the ulcer, using five such needles in each location. At the end of seven days (168 hours) the needles were removed and boric ointment dressings applied. At the end of six weeks a small crust was observed in the center of the treated area. At the end of three months the lesion was smoothly healed, and a depressed scar had replaced the lesion. At the end of six years the appearance was unchanged.

Case 11. (Fig. 6) A. L. W., male, aged sixty-nine, applied for treatment of a cauliflower tumor of the left ear. It started as a crusted ulcer on the upper portion of the pinna about two years before admission and had grown steadily. The entire pinna was included in the cauliflower mass and induration extended into the skin both in front of and behind the ear. A single enlarged node about 2 cm. in diameter was felt in the upper cervical region, just below the ear. The ear was smoothly removed with a high frequency needle leaving a layer of malignant tissue at the base of the pinna having a thickness of approximately 0.5 cm. The pathological report on tissue removed was epidermoid carcinoma, squamous cell type, Grade 2.

Twelve 1.33 mg. radium needles were inserted 0.8 cm. apart under the remaining malignant tissue and well beyond it, and one 2.4 mg. needle and four 1.33 mg. needles were sewed 0.8 cm. apart in and about the cervical lymph node in a plane corresponding to the lymphatics of this region. The needles were left in place for 168 hours and during this period daily doses of

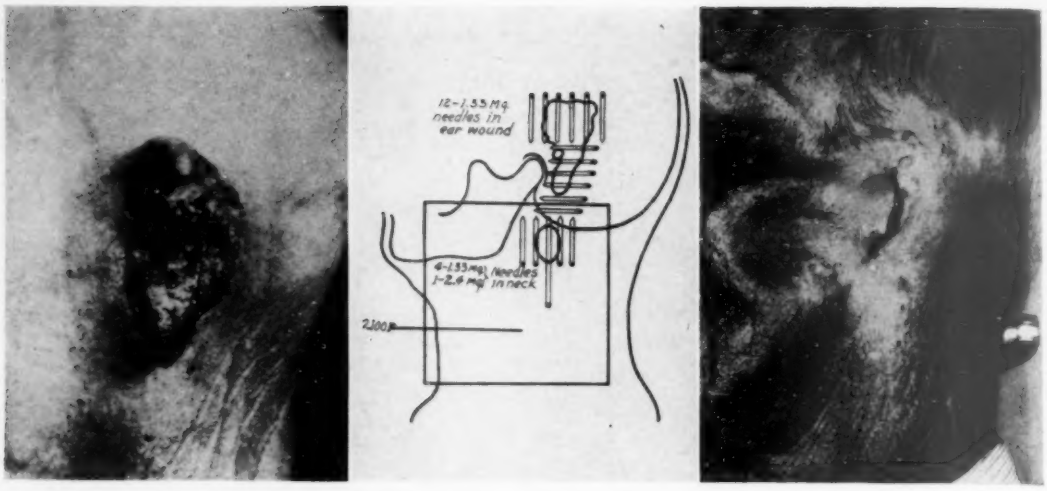


Fig. 6. Large squamous cell carcinoma of ear with extension to surrounding tissues and an enlarged cervical node treated successfully by a surgical reduction of the tumor to a flat slab and a layer radium needle implantation.

roentgen rays (350 r) were administered to an area measuring 10.0 cm. on a side laid out over the upper cervical region to include the enlarged node. The treatment factors were 220 kv., 20 ma., a target-skin distance of 50.0 cm. and a filter of 2.0 mm. of copper and 1.0 mm. of aluminum; the total dosage was 2,100 r.

At the end of six weeks a smooth, clean ulcer was observed at the site of the removal of the ear. At the end of four months the wound was smoothly healed, soft and pliable, and the enlarged node was no longer palpable.

Case III. (Fig. 7) W. E. W., male, aged fifty-eight, applied for treatment of a large cauliflower bleeding tumor involving the lower portion of the left ear, of eighteen months' duration. The projecting portion of the tumor and the lower half of the pinna of the ear were removed with the high frequency needle leaving a layer of malignant tissue having a surface area measuring approximately 5.0 by 7.0 cm., and a thickness varying from 0.5 to 1.0 cm. The pathological report was epidermoid carcinoma, squamous cell type, Grade 4.

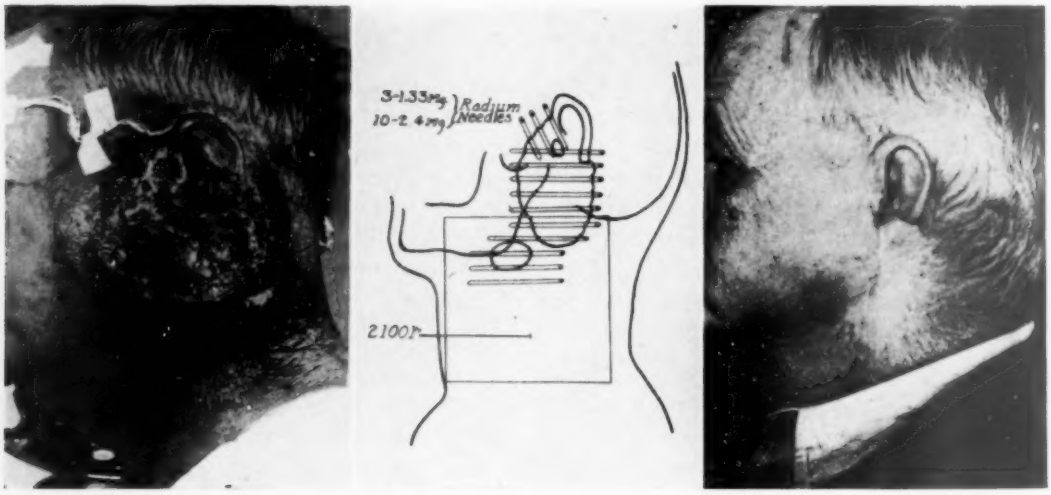


Fig. 7. Appearance of large squamous cell carcinoma of ear and face after removal of half of the ear, a surgical reduction of tumor to a slab, and a layer radium needle implantation. The photograph on the right shows the smoothly healed scar as it appeared two and a half years later.

A hard, movable lymph node measuring about 1.5 cm. in diameter was felt behind the angle of the left jaw. A series of seven 2.4 mg. and three 1.33 mg. radium needles were placed 0.8 cm. apart at the base of the visible malignant tissue and three 2.4 mg. needles were inserted into and alongside the lymph node in the plane of the lymphatics of the neck and 0.8 cm. apart.

A total dosage of 1,750 r was administered to an area measuring 10 cm. on a side, laid out in the upper cervical region to include the enlarged node, using the same factors as those given for Case 11. At the end of seven days (168 hours) the needles were removed and boric ointment dressings were applied. Healing was slow but at the end of five months the wound was smoothly healed and the gland was no longer palpable. This patient has remained well with no evidence of recurrence for two and a half years.

SUMMARY

1. A simple method for estimating dosage in a thin layer of tissue implanted with a single row of radium needles is described.

2. Many carcinomas may be reduced to such layers by electrosurgery.

3. Larger neoplasms may be treated by using several layers of needles.*

* For discussion see page 385.

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PATHOLOGIC ASPECTS OF THE RADIOSENSITIVITY OF MALIGNANT TUMORS*

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WHILE there is little new that I can hope to bring you on this subject, there are still unanswered problems that I would like to recall to you, as they can be solved most readily with your help. As examples of these problems: Why is it that lymphomas will melt away with light irradiation, but the patient will usually die of the disease? Why do the great majority of malignant melanomas fail to respond to irradiation, and yet a rare case be cured by its use? Why does epidermoid carcinoma of the cervix uteri respond well and epidermoid carcinoma of the vulva often fail to respond? Or why does carcinoma of the cervix at times disappear with irradiation, only to recur in a resistant form after a lapse of months?

These questions of radiosensitivity and radioresistance can as yet be answered only empirically; yet, on the adequacy with which they will be answered depend the lives of many of your patients. In order to define the problem, let me present three arbitrary groups. Those tumors which regress noticeably with a dose that does not ordinarily produce appreciable normal tissue damage—the equivalent of 2,500 r or less, delivered to the skin in divided doses at 200 kv.—are classed as radiosensitive. Examples of these are leukemia, multiple myeloma, or lymphoma. Those tumors which respond in the range from 2,500 to 5,000 r—producing definite but not extreme reaction in normal tissues—are classed as radioresponsive. Examples of these are basal cell carcinoma of the skin and benign giant cell tumor of bone. Those tumors which require doses above 5,000 r for regression—which are apt to produce permanent damage to normal tissues—are classed as radioresistant. In this group fall osteogenic sarcoma and malignant melanoma.

Unfortunately, radiosensitivity and radiocurability are not synonymous. Some types of tumor which give a good immediate response are rarely cured. As you all know only too well, radioresistance may be acquired by a previously sensitive tumor.

In any consideration of the response of tumors to radiation therapy, precedence must be given to the type of the tumor cell. In general, the less differentiated the cell, the greater its sensitivity, but exceptions are very numerous. From the clinical standpoint, however, tumor cells cannot be considered apart from their supporting stroma and the normal tissues which they invade. The importance of fibrous tissue and vascular change in tumor therapy is axiomatic. This is perhaps fortunate, for in tissue culture the complete killing of cells by irradiation is difficult. Some fibroblasts in tissue culture may remain viable even after 100,000 r.

The tumor cell varies in its sensitivity, as does its normal counterpart, as the cycle of cellular activity progresses. In general, a cell in mitosis is more sensitive than in the interkinetic phase,[1] and the early prophase appears to be the most sensitive mitotic stage. Some evidence exists that the abnormal mitoses seen after irradiation may be related to effects upon the centriole.[2] Efforts have been made to time the application of radiation to assumed cyclicly recurring periods of maximum mitotic activity, but while waves of mitoses do occur in tumors, their regular recurrence, particularly in tissue subjected to irradiation, is questionable. There is this, however: in at least some tumor cells damaged but not

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killed by irradiation, repair is nearly complete in twenty-four hours.

Since the days of Hertwig[3] the rôle of the nucleus in radiation changes has been stressed. In recent years, Failla[4] and his coworkers have clearly demonstrated cytoplasmic vacuolization and swelling as well as nuclear changes following irradiation.

Normal cells respond to irradiation much as do neoplastic cells, and different tissues vary in their responses much as do different tumors. The fundamental reactions of cells to irradiation are essentially similar, varying in degree rather than in character.

It is perhaps heresy to admit to the members of the American Radium Society that the variations in wave length of radiations commonly used therapeutically seem to make little if any difference in the character of the response of the tumor cell, but the evidence points strongly to the amount of radiation absorbed as the essential factor and the wave length as of minor importance. When one studies the cells of an experimental tumor or a tumor in the human treated with roentgen rays generated at voltages ranging from 120,000 to 1,000,000 volts, with gamma radium rays, with beta rays from radioactive phosphorus, one is impressed by the essential similarity of the changes brought about by these different agents.

Cessation of mitosis, degeneration of cellular structure resulting in cell death, swelling and vacuolization, changes in the Golgi apparatus and mitochondria occur as an almost immediate result of irradiation, with any type used therapeutically, and the later changes due to irradiation also lack specificity. The hyalinization of collagen, the degeneration of elastic tissue, the abnormal cells and altered blood vessels result as later changes of roentgen and radium irradiation alike. It is fortunate that this is so, for the stromal changes and reactions of the normal supporting tissues play an important part in the therapy of any tumor, hindering the nutrition and hampering the spread of those tumor cells surviving the direct effect of irradiation.

In view of the importance of the response of the supporting tissues, it is unfortunate that the idea has grown up in the minds of many laymen that radiation therapy should cause a tumor to vanish but should not produce scars or reactions in normal tissues. The surgeon of necessity produces deformity in cancer therapy and his scars are not questioned; the production of a severe radiation reaction is often necessary to bring about tumor regression, and resulting burns or ulcers though regrettable should be recognized as legitimate by-products of effective eradication of the tumor. This, of course, assumes due regard for such a reaction and its production only if necessary.

When a tumor, which as a result of irradiation has once regressed, does recur, it usually fails to respond appreciably to the dose of radiation which caused its initial regression. By some, this acquisition of radioresistance is ascribed to the failure of the already altered stroma to respond adequately a second time; by others, to an actual selection of radioresistant tumor cells by killing off the sensitive cells of the tumor and so permitting resistant ones alone to develop.

By detailed observation of your cases, paralleled whenever possible by repeated biopsy following irradiation, it should be possible to determine those factors on which radiosensitivity, and hence the success of radiation therapy, depends.

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DISCUSSION ON PAPERS OF DRS. HOWES AND CAMIEL, MARTIN, AND WARREN

Dr. George T. Pack, New York. Evolution in methods of treating cancer by radium and roentgen rays has progressed along three distinct lines during the last fifteen years. The first improvement has been a better and more gen-

eral appreciation of the radiosensitivity of cancers. The selection of tumors of radiosensitive behavior for treatment by irradiation requires a knowledge of the histologic and biologic factors determining radiosensitivity, a familiarity with the natural history of malignant tumors of all regions, and considerable clinical experience in observing the response of these tumors to treatment. In Dr. Warren's evaluation of the factors influencing radiosensitivity he did not mention the relatively great importance of the fundamental nature of the tissue of origin of the tumor. Thus, the primitive blood-forming tissues predetermine the radiosensitivity of tumors developing from their lymphoid, myeloid and vascular derivatives (lymphosarcoma, myeloma, endothelioma, angioma) and the various tissues arising from the neural crest cells almost uniformly give rise to radioresistant tumors (glioma, neurosarcoma, melanoma). The same radioresistance is found in tumors originating from the primitive cells that go to form the supportive framework of soft somatic and osteoblastic tissues. Along with this recognition of radiosensitivity, comes a fuller cognizance of the variations in sensitivity of normal tissues and cancer, the difference in their respective recuperative abilities following irradiation, and a rational application of these advantages by fractionation of doses, cross-firing through multiple portals and other new well known means of destroying the cancer with preservation of normal tissues.

The second great advance has been the effort to deliver greater tissue doses of radiant energy to deeply situated tumors through the medium of higher voltages (supervoltage radiation), heavier filters and greater target-skin distances.

The third trend has been a reversion to lower voltages in apparatus which are definitely superior to the old low voltage equipment in three ways; shock-proof nature, remarkable flexibility, delivery of a huge output in roentgens in a very brief time. I have employed both the Philips and Chaoul machines. In discussing the indications for the use of these instruments, we must seriously ask ourselves if there are any advantages over the conventional methods now in use. In my opinion, the majority of epitheliomas of the skin can be treated equally satisfactorily with the ordinary low voltage units of 100 to 120 kv. or with radium properly applied, obtaining equally good cosmetic results, and equally high percentage of cures.

The economy of the initial cost and expense of treatments are not enough to justify the purchase of the instrument solely on this account, but the other advantages are real and make these instruments worthwhile additions to our armamentaria for radiation therapy. The remarkable flexibility of these applicators is appreciated when they are used in irradiating superficial cancers of the buccal mucosa, lip, floor of mouth, palate, pharynx, vagina and other regions where the position for treatment is awkward and difficult to maintain for any length of time. The phenomenally short time required to deliver an effective dose is particularly helpful in the treatment of hemangiomas in children, and moreover it enables this to be done without undue exposure to the parent or relative who is holding the infant.

My only fear is that these methods of contact or short-distance roentgen therapy may be unjustly discredited by radiologists who attempt to extend the indications for it beyond its capabilities. It is well to be aware of these physical limitations and not to treat tumors which are too deeply infiltrating or too thick, unless the superficial portion of the lesion has first been removed with the endotherm or actual cautery. Many oral cancers are too deeply infiltrating for this method and can be treated with greater prospect of success through peroral cones attached to high voltage roentgen therapy units. The portals or therapeutic fields for both the Chaoul and Philips machines are quite small and circular; an attempt to employ multiple portals to cover a large skin or mouth cancer is usually somewhat inaccurate and necessitates some overlapping of fields.

We have been experimenting with intra-abdominal contact roentgen therapy of inoperable cancer of the pancreas and gastric cardia. We have devised a special metal jacket which may be sterilized and placed over the long proboscis-like tube of the Philips machine; the filter of 2.5 mm. Al is soldered in the end of the metal jacket or cone so that no unsterile part of the instrument may contaminate the peritoneal cavity and wound. The Philips tube may be held by the hands during this intra-abdominal irradiation. The patient is prepared for an upper abdominal operation. When the pancreatic or gastric cancer has been exposed and found to be unresectable, the size and extent of the tumor are estimated and the surface to be treated is divided into the number of fields considered necessary. Each field is given a dose of 4,000 to 5,000 roentgens, with the factors of

2 cm. distance and 2.5 Al filter. The output with this set-up is 550 r per minute. In some instances the stomach is opened and, through the gastrotomy, a similar dose is given within the cavity of the stomach against the mucosal surface of the tumor. End-results are not available for this new method of treatment. There should be very little danger of peritonitis with the sterile technique as practiced. The entire duration of the radiation treatment is from thirty to forty-five minutes, which is not prohibitive. The reactions to date do not seem to be more severe or protracted than those produced by external irradiation with the fractionated technique.

We also conceived the scheme of making cancer of the urinary bladder accessible not for a short time as at cystotomy, but over an extended period of many days or several weeks, and by treating the cancer thus exposed by repeated fractionated doses of low voltage roentgen radiation applied at a short distance. This method of treatment consists of (*a*)marsupialization of the urinary bladder, (*b*) endotherm excision of the bulk of the cancer when possible, and (*c*) maintenance of an opening into the bladder so that the low voltage Chaoul tube may be repeatedly inserted against the cancer at the bladder base. Our brief experience with this method has convinced us that it has many advantages. Marsupialization of the bladder is effected by suturing the bladder mucosa to the suprapubic skin and the maintenance of this large opening by the constant wearing of a large Marion drain. Four or five days are allowed to elapse to insure a definite anchoring of the bladder to the abdominal wall. Sterile precautions are taken during each treatment. Cones attached to the Chaoul tube permit a 5 cm. target-tumor distance; the cone is inserted within the urinary bladder in the desired position and the tube stand is then manipulated so that the anode end of the tube can be slipped into the open end of the cone. A dosage of 2,500 r is then given every other day until nine or ten such treatments totalling 22,500 or 25,000 r are given over a period of eighteen to twenty days. The bladder is kept open and the cancer is palpated at the time of each treatment and for three to six weeks after consummation of the treatment, so that the regressing cancer can be frequently inspected and cleaned. The cystostomy is later closed by a minor operation.

It may be an unwise prophecy but I rather anticipate the time when we will have tiny, low voltage roentgen units, possibly as small as a pencil, that may be introduced by means of long flexible cables into such organs as the esophagus, larynx, nasopharynx, cervical and uterine canals and deliver intensive local irradiation in such short periods as to supplant intracavitary radium therapy.

Dr. Edith H. Quimby, New York City. It has been recognized for a long time in interstitial as well as in external therapy that we must know the amount of radiation that gets to the point which we are trying to treat. We have said that a good many times and we will probably say it a good many times more.

In interstitial therapy it is much more difficult to arrive at any satisfactory method of doing this than in external. I think the first attempt was reported by Dr. Hayes Martin and myself before this Society in 1929. The work that we presented at that time was based on a combination of clinical and biological experimental work and a tremendous amount of arithmetic, and was the beginning of the sphere method that Dr. Charles Martin spoke about and that Dr. Hayes Martin, Dr. Pack and I later elaborated on.

In the years since then a number of other people have approached the problem from a number of other ways. Dr. Martin has referred to Dr. Laurence's work but he has neglected to mention the extensive and valuable work which has been done abroad. In 1931 Sievert in Stockholm published some charts and tables which were almost identical with the ones Dr. Martin has showed this morning. A little later Dr. Mayneord in London published somewhat similar ones and then, in the course of the next few years, Paterson and Parker in Manchester published a series of studies on dosage in interstitial irradiation which in part, at least, were based on almost exactly the same layer method that Dr. Martin has worked out independently.

Paterson and Parker's data give tissue doses in terms of gamma roentgens. The American data, particularly ours, has continued to give it in terms of erythema doses until very recently. The erythema dose, as you all know, is a clinical and approximate unit; it is based on experimental observation of the amount of time that it takes certain applicators to produce a skin reaction.

Within the last few years, the gamma-ray roentgen has been standardized and it is now possible to relate doses in terms of the two units by means of certain experimental work.

The conversion factor is 1 threshold erythema dose equivalent to 1,000 gamma roentgens.

All of the information in the literature, whether it is Swedish or English or American or Canadian, is based on the same fundamental assumptions and the same fundamental curves, and therefore it would be strange if it didn't all agree. However, it is always a satisfaction to have a fresh and independent check on one's arithmetic, and Dr. Martin has just furnished us with another.

DR. EUGENE P. PENDERGRASS, Philadelphia. I feel that the American Radium Society is very fortunate in having Dr. Shields Warren talk to us on this vital subject. He is a man who has had a large experience on which he can call.

Dr. Warren states that if we do repeated biopsies it should be possible to determine those factors on which radiosensitivity and hence the success of radiation therapy depends. This is a very important statement and I therefore would like Dr. Warren to elaborate on his suggestion. How often should we take the biopsies? From what part should the tissue be taken? Should the biopsy include any normal tissue? Is it his idea that the pathologist should describe the microscopic appearance and an effort be made to correlate it with the clinical findings as to response and type of radiation reaction?

Dr. Warren states that "the production of a severe radiation reaction is often necessary to bring about tumor regression, and resulting burns or ulcers, though regrettable, should be recognized as legitimate by-products of effective eradication of the tumor."

Such statements should assist greatly the radiologists who are annoyed by the medicolegal aspects of such reactions. If the general medical profession could be informed concerning the attitude that has been expressed and emphasized by Dr. Warren, I believe that radiologists would be less likely to undertreat some tumors.

There are two other questions which have some bearing on the subject matter under discussion that I would like Dr. Warren to comment upon. Does he believe that irradiation may traumatize tissues in such manner that the malignant process will take on more rapid growth characteristics? Is there a general body influence on the growth of tumors which may be present at one time and not at another?

For instance, Ferguson, in a review of 258 cases of osteogenic sarcoma in the Registry of Bone Sarcoma, treated by amputation, found that only 8 per cent survived early amputation and 29 per cent survived late amputation, being done six months after the onset of symptoms. Has Dr. Warren had an experience similar to that of Dr. Ferguson, and if so, does he have an explanation?

Dr. Howes and Dr. Camiel have prepared a comprehensive review of their experience in the treatment of the first 100 cases treated at the Brooklyn Cancer Institute.

The authors emphasize that this method of therapy has the advantage of convenience, speed and economy. They state that the cost per treatment with the present therapy is estimated at less than one dollar. I believe that the authors should tell us how the cost was arrived at. Does it mean that one could charge two dollars for the treatment of an epithelioma of the lower eyelid and make 100 per cent profit?

Not enough importance is given to the problem of protecting the operator from the rays scattered from the Philips apparatus. According to Mayneord, the tolerance dose to stray radiations emitted during short distance low voltage irradiation is 0.0006 r per minute. According to the figures given by these authors, the stray radiation from the Philips apparatus is about 33 times the safe limit. In order to overcome this objection of lack of protection, we are arranging to put a swinging lead door on the cabinet of the Philips apparatus to protect the operator.

The authors call attention to the high output of the Philips apparatus. They state that with such high intensities it is extremely difficult to administer small doses accurately because of the timing device. In order to overcome the inaccuracy of timing for short applications, would it not be possible to lower the milliamperage in addition to the measures that they are now employing?

The authors routinely use 10,000 to 13,000 r at one sitting (dosage in air; no backscatter). They have already had several indolent ulcers. That was our experience even though we used smaller fractionated doses. I think an increase in the number of ulcerations may be encountered in cases two or three years after treatment. I agree that cartilage does not tolerate radiation well, but if the doses are fractionated and reduced, less chondritis will occur.

I have seen one patient who had interference

with nasolacrimal drainage after treatment of an epithelioma in that vicinity. This is an annoying complication and apparently develops after a large amount of radiation.

In treating cancer of the face or of any part —any cancer that is ulcerated and secondarily infected— my experience has led me to believe that in the beginning one should treat the lesion as an infection first and then treat the malignancy. I believe I have seen metastasis instituted following heavy initial treatments in patients with ulcerated carcinoma of the lip.

In treatment of hemangiomas very satisfactory results may be obtained from small doses such as 125 r. I would advise against the larger doses. Another important factor is to treat the patient in the first three months of life.

There are many conditions that may be treated with this apparatus, but those lesions occurring around the eye are particularly suitable.

Dr. Hayes Martin, New York. Dr. Howes' report on contact radiation therapy seems to me to be an example of a common tendency among the medical profession to extol the merit of some new apparatus on the basis that it does something equally as well as an already existing apparatus. So far as I can see, Dr. Howes presents no data which indicate that the contact therapy can produce any better or, as a matter of fact, any greatly different effects from those produced by our already existing 100 kv. low voltage apparatus. Dr. Howes has emphasized that one of the main advantages of contact therapy is the saving of time, which on closer examination proves to be a relatively minor matter. With the ordinary low voltage roentgen machine properly adjusted and equipped, a target-skin distance of 15 cm. or even less can be used and doses of several thousand roentgens can be given in four or five minutes. When it has taken ten or fifteen minutes to get the patient ready on the treatment table, the shield prepared, and the machine adjusted, it seems to me that it is a matter of minor importance whether the actual treatment time is one minute or five.

So far as treatment of skin cancer is concerned, it seems to me that the Philips contact therapy apparatus is rather insecure. The danger of exposure to the operator, the chance that the unstable tube will move during treatment, and the variable dosage that may be given depending on variations of 1 to 2 mm. in placing the tube seems to us to counteract any theoretical advantages of this machine. Possibly in the future some of these clinical difficulties will be overcome.

Dr. Charles Martin's report of the layer technique in radium therapy is built around his use of radium needles, and I think that he has worked out an excellent plan for this form of radium applicator. On the other hand, I think that his method of calculating dosage would be unsuitable for radon seeds. Furthermore, I got the impression that he was presenting this method of dose computation in competition to the sphere method. You will note, however, that most of his cases were superficial—that is, they were thin, flat cancer of the skin of the face, and if they were bulky, he first shaved them down to make them flat. The sphere method is, of course, not applicable to these thin lesions, and Dr. Quimby and I did not present it as the solution for that problem. In the radiation therapy of large masses—for instance, neck nodes—it seems to me that the layer technique and the sphere method aim at accomplishing the same purpose in different ways, but that by the layer method Dr. Martin is using a two-dimensional method to solve a three-dimensional problem. Nevertheless, it is probable that if a physicist calculated required dosage by the layer method and by the spherical method he would obtain about the same figures.

I have personally long been interested in more accurate systems of dosage calculation, but I must confess that most of them work better for the physicist than they do for the clinician. The physicist with his instruments of precision, both physical and electric, and with accurate mathematics, including calculus, can figure out dosage requirements in distances of millimeters and fractions of millicuries to several decimal points, but the clinician treating a mass in the neck must estimate the size of the mass, select a dose of millicuries from a table, and then attempt to place the seeds geometrically within the inner half of the radius of the mass.

All this may seem very exact and scientific but, between you and me, it can't be done accurately. None of us can measure a mass of cancer accurately except in the pathology laboratory with the help of the microscope, and the selection of the number and the total dosage of the seeds must therefore be approximate. Dr. Quimby and I made our calculations of

tissue dosage in masses on the basis that the seeds were placed within the inner half of the radius; practically, that again can only be approximated. When the seeds are placed in the neck node through punctures in the skin, I think one is very lucky if all of the seeds even go inside the mass. Still, Dr. Quimby and I admitted these inaccuracies in our work. On the theoretical basis we calculated a dose of 4 to 5 S.E.D. as lethal for squamous carcinoma, but we did not advise giving such moderate dosage. We recommended giving 7 to 10 S.E.D. since we conceded that the ideal accurate placement of sources was impossible.

I wish to call attention to the apparent impossibility of correlating the sphere method of dosage calculation with Dr. Charles Martin's layer technique. If I do not misunderstand, Dr. Martin has calculated the interstitial dosage requirements in a given rectangular solid by the sphere and by the layer techniques, respectively. With the sphere technique he calculated the dose as 5 mc. of radium and by the layer technique 1,500 mc-hr. On this basis he would give over twice as many millicurie- or milligram-hours by a layer technique as would be required by the sphere technique. I don't know where the discrepancy lies, but it is apparently difficult to correlate the two methods.

Dr. Warren's presentation is a timely one, and we are fortunate in having before this Society such a discussion on the histopathology of radiation effects. I hope that we shall have more of these in the future. Dr. Warren, a pathologist, discusses radiation effects as seen under the microscope in terms of radiation dosage, which is something new in my experience.

I think it unfortunate, however, that Dr. Warren has given his dosage in roentgens on the skin without mentioning the portal size. The same error has been made yesterday and today in other papers. I should like to call attention again to the fact that the dosage in roentgens on the skin is of very little significance unless the portal size is also given, and I trust Dr. Warren can add these factors to his published report.

JAMES L. WEATHERWAX, Philadelphia. There is a phase of contact therapy that I would like to discuss. The question arises from time to time as to the relative number of roentgens one should deliver as a surface dose in the use of the Philips compared to Chaoul therapy tube.

If the arrangement of the roentgen tube in Philips and Chaoul therapy is the same, that is, at a 3 cm. target-skin distance, at 3 cm. in the tissue or 6 cm. from the target, there should be a loss in intensity of 75 per cent due to the spread of the rays following the inverse square law. This is the same for both types of equipment. There is an additional loss due to the absorption of the 3 cm. of tissue through which the rays have passed. Here is where the Chaoul and Philips therapy differ. The Chaoul therapy equipment has a filter of approximately 0.2 mm. Cu. equivalent, while the Philips therapy equipment has approximately unfiltered radiation, or equivalent to about 0.5 mm. Al.

According to Mayneord, Chaoul contact therapy at a 3 cm. target-skin distance delivers about 17 per cent of the surface dose at 3 cm. in the tissue. Therefore, if the tumor bed lies 3 cm. beneath the surface of the lesion, 17 per cent of the surface dose is effective at that depth.

Philips contact therapy with 3 cm. target-skin distance and only inherent filtration delivers 9 per cent of the surface dose at 3 cm. in the tissue.

If the radiologist wishes to deliver a given number of roentgens to a tumor base, it is therefore important to think in terms of percentage depth dose. It is readily seen that in order to deliver the same depth dose to a tumor bed, a greater surface dose will be required for Philips than for Chaoul contact therapy. Therefore, dosages delivered to the surface of the lesion in any contact therapy setup will depend upon the depth dose, and that will depend on the target-skin distance and the quality of radiation.

DR. GIOACCHINO FAILLA, New York City. Not being a pathologist I rise with great trepidation to discuss one of the many important points that Dr. Warren has brought out in his paper, namely that of acquired radioresistance. It seems to me that there are three ways in which it can be brought about. One is by the modification of the normal tissues around the tumor due to the first radiation treatment whereby circulation is interfered with, and we know from general experience that when circulation is poor the tumor response to irradiation is also poor. The second way mentioned by Dr. Warren is that if the less resistant cells of the tumor are destroyed and what remains are the more resistant cells, perhaps the tumor itself when it recurs is more radioresistant. A third possible way is by the occurrence of a mutation

so that the tumor becomes really of a different type, which might be more radioresistant.

It is very important to know which one of these three processes really applies to this problem because if it is a question of mutation or the selective destruction of the sensitive cells, there is little or nothing we can do to change the situation. On the other hand, if it is a question of interference with circulation, there is perhaps something we can do. For one thing, in giving the first treatment we might irradiate as little normal tissue as possible in the hope of interfering as little as possible with circulation in case a subsequent course of treatment becomes necessary. One may also be able to improve the circulation by some as yet untried artificial means when the recurrent tumor is irradiated.

Therefore I think every attempt should be made to decide which one of these three processes brings about the so-called acquired radioresistance.

Dr. Howes (closing). In my paper I tried definitely to emphasize the limitations of the contact type of apparatus. I want to thank Dr. Pack for his discussion, particularly his vision into the future, which may or may not be true. Certainly we are attempting to get our radiant source down to the tumor as illustrated by intravenous injections of radioactive phosphorus and other methods in comparison with older techniques.

With regard to the economics which I discussed in the paper, I think that this is an important phase of the question. Certainly the treatment of cancer is an economic problem to the patient and anything that will cut down the cost of the treatment should be seriously considered by the medical profession.

As to late ulceration, I have a different opinion than Dr. Pendergrass. If you noticed on the lantern slides these scars lacked any evidence of telangiectasia. Again I wish to emphasize the absorption of the radiant energy in the superficial layers and the consequent preservation of the tumor bed.

Dr. Charles L. Martin (closing). I wish to thank Dr. Quimby and Dr. Hayes Martin for their discussion. I discuss technical subjects with some trepidation when Mrs. Quimby is present and her willingness to accept my calculations is most gratifying.

It is true that I omitted some of the foreign literature but, to the best of my knowledge, no chart of the type included in my paper has been published. Certainly no such chart is included in Cade's book which is just off the press and which describes radium needles similar to those used in our clinic.

As Dr. Hayes Martin pointed out, the extreme accuracy of implantation which seems indicated by physical calculations is not always essential to the production of good clinical results, and in practice the patterns are never perfect. However, a simple plan of dosage calculation is very helpful.

Dr. Warren (closing). There are a number of points that I would have been glad to cover had I had time available. I appreciate very much the kindness of the discussers in giving me an opportunity to bring out some of them.

One point which I did neglect and which Dr Pack very kindly brought out for me is the tendency of cells derived from various embryologic sources to behave somewhat in the same way when they make tumors. However, one cannot be guided entirely by this. There are enough exceptions to this general rule so that we have to supplement the general theoretical foundation with a good deal of empirical knowledge as well. It is a good deal like a man attempting to bring a steamer up into New York Harbor. He could do it reasonably well with a road map, as far as the lay of the land goes, but he would probably strike some shoals and some reefs. If he has a more detailed chart, he can hope to get his steamer in more safely.

With regard to Dr. Pendergrass' question relative to repeated biopsies, I think that with a fairly accessible tumor such as the carcinoma of the cervix—on which most of my work has been done, with the cooperation of Dr. Meigs,—one can get daily biopsies quite readily without appreciable inconvenience to the patient and without apparently doing any harm, judged by the end-result, to the patient.

Of course, there are times when one has to take biopsies a good deal further apart, and I think in general if one can get a biopsy say five to ten days after the initiation of irradiation, then again at the close of the period of radiation, then say six weeks and three months after that, a great deal of information can be gained.

Of course, it is important to correlate this with the clinical appearance of both the tumor and the surrounding normal tissues.

A while ago in a series that we carried

through with Dr. Meigs, with the help of Dr. Severance and Dr. Jaffe, we were able to predict with a fair degree of accuracy, by the time we had our ten day biopsy, whether or not that patient was going to respond favorably to radiation therapy. The point that radiation may traumatize the tissue in the sense of lowering the resistance is a very difficult one to determine. I believe that it may be possible, but I have yet to see any convincing evidence of that.

Tumors vary in their growth rate from time to time and what the determining factors are we cannot say with any degree of accuracy.

With regard to the general body influence, I would prefer to leave that point aside since I know that Dr. Oughterson is going to discuss that with you a little later.

With regard to the observations that Dr. Ferguson reported on the osteogenic sarcoma, I think this point should be brought out: Those were not serial cases but they were cases selected from the Bone Tumor Registry and it is natural for surgeons as it is for radiologists and for pathologists to give comparative conspicuousness to their successes rather than to their failures, and consequently, one finds in the Registry of Bone Sarcoma a higher proportion of successful cases than of failures,—than one would find in a general hospital series.

I believe that these cases were also somewhat artificially selected in that there is variation in the degree of malignancy in osteogenic sarcoma, and I am quite certain that any osteogenic sarcoma that survived the treatment given to some of those reported must have been of very low malignancy indeed.

With regard to the measurement of the dosage that I showed, those were given on the basis of 200 kv., measured in air and for a 10 by 10 cm. or 10 by 15 cm. field. Many of my observations, I have already said, were taken on the basis of carcinomas of the cervix uteri. Those cases were treated at 200 kv. with filtration of 0.5 mm. copper and 1 mm. aluminum, 50 cm. focal distance, 10 by 15 cm. field, cross-firing using four portals, 150 r to each of two fields per day.

I was very much pleased that Dr. Failla brought up the point of acquired resistance. This is one of utmost importance to all of us. I had rather preferred to avoid the consideration of mutation, inasmuch as mutation as we understand it from the geneticist's standpoint rests on chromosomal abnormalities.

There are so many chromosomal abnormalities in tumors whether treated or not, that I think we would have a hard time to speak the geneticist's language here. That there may be alteration in cellular constitution I think is very likely but that it occurs in the same sense in which the geneticists have used the term mutation I am a little uncertain.

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Forty-third Annual Meeting: Palmer House, Chicago, Ill., Sept. 15–18, 1942.

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Representatives on American Board of Radiology: Douglas Quick, New York, N. Y., B. P. Widmann, Philadelphia, Pa., F. W. O'Brien, Boston, Mass.

Twenty-eighth Annual Meeting: 1943, to be announced.

EDITORIALS

RELATION BETWEEN FATS AND GASTRIC INHIBITION

FROM the earliest days of roentgen-ray studies the motor phenomenon connected with the gastrointestinal tract has been of great interest. Numerous investigators have contributed work which has greatly increased our knowledge of this mechanism, many working with various types of foods, both simple foods and combination of foods, in order to determine the function of the pylorus and its mode of action. It has been known since the days of Aristotle that fats inhibit gastric digestion, but the first accurate report of this phenomenon was given in 1833 by Beaumont long before the discovery of the x-ray. He prepared tables of the digestibility of various foods based on the length of time they remained in the stomach. Since Beaumont's time a number of workers have reported detailed observations on the inhibition by fat of gastric secretion. Ivy and his collaborators have shown that this inhibition is partly dependent on the inhibitory hormone known as enterogastrone, which is apparently released from the duodenal mucosa when neutral fat or fatty acids reach that region and are absorbed into the circulation. It is also well established that the ingestion of fat will inhibit both the motor and secretory mechanisms of the stomach. Why such an inhibitory mechanism exists is not well known and relatively little is known about the relation between the chemical structure of a fat and its ability to induce inhibition, though many observers have noted that different types of fat leave the stomach more rapidly than others.

Quite recently Tidwell and Cameron[1] have studied the relation between the chemical structure of fats and their ability to produce gastric inhibition. These investigators, working with cats and rats, found that the more unsaturated fats tended to remain longest in the stomach, while the more saturated ones tended to cause least gastric inhibition and to progress farther down the intestinal tract in a given time. They found that 43 per cent of a dose of olive oil could be recovered from a cat's stomach at the end of three hours, and only 25 per cent of a dose of tripalmitin, but as much as 71 per cent of linseed oil could be found in the stomach at the end of the same period of time.

In order to more easily study the rate of the progress of the fat through the digestive tract, these observers stained fat with Sudan III before homogenization. When the animals were sacrificed three hours after the administration of a test meal much of the tripalmitin was found in the cecum; none of the linseed oil had by that time reached the cecum, indicating that the more saturated fats which show the least gastric inhibition and the least retention in the stomach tend to pass down farthest in the intestinal tract.

Tidwell and Cameron extended their observations further in order to determine whether such findings were valid for man; consequently a number of observations were carried out on a convalescent infant. This infant was given a barium meal containing one or another type of fat—a tripalmitin-tristearin mixture, butter fat or olive oil. Following the administration of this test feeding, which was always given on

[1] Tidwell, Herbert C., and Cameron, Eugenia S. The relation between the chemical structure of fats and their ability to produce gastric inhibition. *Bull. Johns Hopkins Hosp.*, April, 1942, *70*, 362–369.

an empty stomach, roentgenoscopic observations were made at frequent intervals, the time required for the last of the barium to leave the stomach being taken as a measure of the degree of motor inhibition caused by the fat. From these experiments Tidwell and Cameron again found that the gastric emptying time when olive oil was used was twice as long as when a tripalmitin-tristearin mixture was given. Thus the observations on the human confirm those that were made on cats and rats.

Macy, Reynolds, Souders and Olson[2,3] made a roentgenographic study of the gastrointestinal response of a group of seven healthy children whose ages ranged from seventy-four to 117 months. Their dietary, physical routine, and environment, comparable with those of the average, well child in an adequate home situation, were kept as constant as possible throughout all the studies. These investigators found that the administration of a milk meal stimulated considerably more tone and vigorous peristalsis with churning effect in the stomach and a prolonged emptying time and also that the presence of milk in the barium meal caused a delay in the passage of the barium meal through the intestinal loops, particularly in the ileal portions. They also observed that there were great variations in the response of the various subjects to the milk-barium meal.

It was found by Tidwell and Cameron that gastric inhibition tends to increase with the iodine value of the administered fat although the relation between them is not a linear one. Linseed oil, for example, with an iodine value more than double that of olive oil causes only a small increase in gastric inhibition. When, however, they compared the available data on gastric inhibition by different fats with the intestinal absorption of these same fats, they found a striking parallelism.

The results of their studies led Tidwell and Cameron to conclude that the phenomena of gastric inhibition are precipitated by absorption of some fat from the upper intestine, presumably followed by the liberation of enterogastrone, rather than by any physical property of the fat itself; that fat splitting is a prerequisite for fat absorption and this likewise seems to be necessary to produce gastric inhibition.

The exact purpose of the gastric inhibitory mechanism remains obscure; some have thought that the inhibition of gastric motility serves the purpose of permitting the fat to enter the intestine no more rapidly than it can be absorbed, and the experiments of Emery would tend to support this view. Other observers have advanced the opinion that the motor inhibition serves the purpose of preventing hunger, and Sherman in support of this calls attention to the difficulties experienced by the German troops during the first World War when a scarcity of fat prevailed. The rapid emptying of the stomach due to the absence of fat brought about hunger pains soon after the meal was eaten.

The function of the secretory inhibition, Tidwell and Cameron say, is less easily explained. Thomas and Crider suggested that the more rapid discharge of acid into the duodenum, such as might occur in the absence of fat in the diet, might make it difficult to maintain the alkalinity of the duodenal contents needed for the optimal function of the pancreatic enzymes.

Slowly but gradually the riddle of the motor as well as the secretory mechanism of the gastrointestinal tract is being solved. There remains, however, a great deal of work to be done and it is on such fundamental observations as those of Tidwell and Cameron, and others, that the final solution of the problem rests.

[2] Macy, Icie G., Reynolds, L., Souders, Helen J., and Olson, Mary B. Normal variation in the gastrointestinal response of healthy children. Am. J. Roentgenol. & Rad. Therapy, 1940, *43*, 394–403.

[3] Reynolds, L., Macy, Icie G., and Souders, Helen J. Gastrointestinal response of children to test meals of barium and pasteurized, evaporated, and base-exchanged milks. *J. Pediat.*, 1939, *15*, 1–12.

Underwood & Underwood

MAXIMILIAN J. HUBENY
1880–1942

IN THE death of Maximilian J. Hubeny roentgenology has lost another of its pioneers who played a prominent part in the development of that specialty. He died suddenly on July 2, 1942, of a heart attack at Cook County Hospital at the age of sixty-one.

Dr. Hubeny graduated from the Hahnemann Medical College in 1906 and from the University of Illinois College of Medicine in 1909. After several years in general practice in Chicago he took up roentgenology at Cook County Hospital and subsequently served as roentgenologist at the Henrotin,

Chicago Policlinic and Municipal Tuberculosis Hospitals and the Illinois Post-Graduate Medical School. For the last six years he has been Director of the Roentgen Department of Cook County Hospital and was Professor of Roentgenology of its Post-Graduate School.

During the thirty years of his activity in roentgenology he contributed over fifty articles to the literature covering many phases of the diagnostic and therapeutic application of roentgen rays and their rôle in medicine. He was Editor of *Radiology* from 1923 to 1931 and Associate Editor of the *American Journal of Cancer*, the Italian journal, *Radiologica medica*, and the Cuban journal of radiology. His interests were not confined to his specialty but embraced the whole field of medicine and he was almost constantly serving on some local or general committee to advance the interests of his profession.

He was a fellow of the American College of Radiology, the American College of Physicians, the American Medical Association, and the Chicago Roentgen Society and a member of the American Roentgen Ray Society, Radiological Society of North America, Chicago and Illinois Medical Societies, Bohemian and German Medical Societies of Chicago and a diplomate in roentgenology of the American Board of Radiology.

He served as President of the American College of Radiology, Radiological Society of North America, Chicago Roentgen Society and Alumni of the University of Illinois College of Medicine. He was also Chairman of the Section of Radiology of the American Medical Association. The Radiological Society of North America awarded him its gold medal for meritorious service in 1931.

Personally he was a most likeable individual who endeared himself to those with whom he came in contact. His guiding influence has benefited many and will ensure an enduring memory. His innumerable friends will miss him sorely.

ADOLPH HARTUNG

HENRY WALLACE GROTE
1869–1942

DR. HENRY WALLACE GROTE, a member of the American Roentgen Ray Society since 1918, died at his home in Bloomington, Illinois, on June 20, 1942. He was born in Wheaton, Illinois, in 1869, and attended Wheaton College and Northwestern University, receiving the degree of Ph.G. from the latter in 1891. He received his M.D. degree from Rush Medical College in 1894, and from 1894 to 1897 practiced medicine in Chicago. In 1898 he studied surgery at the New York Polyclinic and for the next three years was in general practice in Wheaton and was county physician of Du Page County. In 1901 he located in Bloomington. His active connection with roentgenology began in 1898, and he gave his exclusive attention to it from 1912 on. His left hand bore the mark of the x-ray pioneer, having lost part of three fingers. He was a charter member of the Radiological Society of North America, and was a member of numerous other medical societies, and the American College of Physicians. He was a founder and the first president of the Illinois Radiological Society.

He is survived by his wife, Mrs. Florence Hubbard Grote, to whom he was married in 1897, and by his daughter, Florence Louise (Mrs. M. George Harbula) of Wheaton, Illinois.

Members and Visitors Attending 19th Annual Meeting of the American Roentgen Ray Society,
Camp Greenleaf, Chickamauga Park, Georgia, September 4, 5 and 6, 1918.
Major Willis F. Manges, President and Director, Military Roentgenology.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual Meeting: Palmer House, Chicago, Ill., Sept. 15–18, 1942.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Annual meeting: 1943, to be announced.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: 1943, to be announced.

ARKANSAS RADIOLOGICAL SOCIETY
Secretary, Dr. J. S. Wilson, Mack Wilson Hospital, Monticello, Ark Meets every three months and also at time and place of State Medical Association.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Drake Hotel, Chicago, Ill., Nov. 30–Dec. 4, 1942.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

SECTION ON RADIOLOGY CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. J. D. Coate, 434 Thirtieth St., Oakland, Calif.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL ASSOCIATION
Secretary, Dr. Donald R. Laing, 65 North Madison Ave., Pasadena, Calif. Meets on second Wednesday of each month at the County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N.Y. Meets monthly on fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N.Y. Meets second Monday of each month except during summer months.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. Warren W. Furey, 6844 S. Oglesby Ave., Chicago, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. Samuel Brown, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, J. O. Newton, 13921 Terrace Rd., East Cleveland. Meets at 6:30 P.M. at Midday Club on fourth Monday each month, October to April, inclusive.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. Edward J. Meister, 366 Metropolitan Bldg., Denver, Colo. Meets third Friday of each month at Denver Athletic Club.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Walter A. Weed, 204 Exchange Bldg., Orlando, Fla. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month at a place designated by the president.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meeting held the second Sunday in May annually.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in April.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

LOUISIANA RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society meeting.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. E. M. Shebesta, 1429 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. C. A. H. Fortier, 231 W. Wisconsin Ave., Milwaukee, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Hugh F. Hare, Lahey Clinic, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. H. J. Perlberg, 921 Bergen Ave., Jersey City Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. M. M. Pomeranz, 1020 Park Ave., New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. L. A. Nash, St. John's Hospital, Fargo. Meetings held by announcement.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Ohio Radiological Society
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

Pacific Roentgen Society
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

Pennsylvania Radiological Society
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport.

Philadelphia Roentgen Ray Society
Secretary, Dr. B. R. Young, Temple University Hospital. Meetings first Thursday of each month from October to May inclusive at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

Pittsburgh Roentgen Society
Secretary, Dr. R. G. Alley, 4800 Friendship Ave. Meets second Wednesday each month, 4:30 P.M., October to June, Pittsburgh Academy of Medicine.

Rochester Roentgen Ray Society, Rochester, N. Y.
Secretary, Dr. Sidney Larson, Strong Memorial Hospital. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

Rocky Mountain Radiological Society
Secretary, Dr. A. M. Popma, 220 N. First St., Boise, Idaho. Annual meeting scheduled for Denver, summer of 1942, has been cancelled.

St. Louis Society of Radiologists
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of each month, except June, July, August, and September, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. H. A. Hill, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months at Toland Hall, second at Lane Hall.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. L. W. Baird, Scott and White Clinic, Temple, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00-5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. C. H. Peterson, 603 Medical Arts Bldg., Roanoke, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday each month, College Club, Seattle.

X-ray Study Club of San Francisco
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly in evening on third Thursday.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1 England.

Section of Radiology and Medical Electricity, Australasian Medical Congress.
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
Secretary, Dr. A. D. Irvine, 540 Tegler Bldg., Edmonton Alberta.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N.S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse Biel. Meets annually in different cities.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

BULLETIN OF THE AMERICAN COLLEGE OF RADIOLOGY

MODEL CANCER BILL

"A State law making cancer a reportable disease is essential in order to furnish students of the cancer problem with facts which cannot be obtained from laboratory studies but can be obtained by broad studies of cancer as it occurs in the population at large." Thus summarized a special Cancer Survey Commission created by the New York State Legislature in 1939. As a result of the Commission's studies and recommendations, New York enacted in that year a law requiring physicians to report to the State Department of Health all cases of cancer coming to their attention.

Cancer is a reportable disease in 17 of the 48 states. Reports are made compulsory by regulation of the state department of health in 14 of these. In the remaining 3—New York, Wisconsin and Rhode Island—special statutes have been enacted.

A proposal that the American College of Radiology encourage the compulsory reporting of cancer cases was submitted to the Board of Chancellors at its regular meeting in February, 1942. Following thorough discussion by both proponents and opponents, the Board referred the question to a special committee for further study with instructions to submit a report at the June, 1942, meeting of the Board. At that meeting the special committee, composed of Dr. Lewis G. Allen, Chairman, Dr. Arthur W. Erskine and Dr. James J. Clark, recommended that the College sponsor a model bill making cancer a reportable disease.

In its report, the committee expressed the opinion that organized radiology, as the group most interested in the problem of cancer, should take the lead in sponsoring sound public health measures designed to furnish statistical information concerning cancer. A constructive effort in the interest of the public health which would stimulate lay education was both a logical and laudable project for the American College of Radiology, the committee said. The practice of quacks who dupe patients with false diagnoses of cancer would be discouraged if all such cases were required by law to be reported, the report pointed out. The committee recommended that public health regulations or special statutes be sponsored in the 31 states where cancer is not now reportable.

The Board of Chancellors approved the report of its special committee and instructed the Commission on Legislation to sponsor the enactment of uniform laws or regulations in all states through the Councilors of the College. Where legislation is necessary, the committee recommends the following model bill:

> Section——. Any physician or other practitioner knowing that a patient treated or examined by him has cancer, carcinoma, lymphoma, sarcoma, leukemia, or any other form of malignant growth shall report the same promptly to the ——— Bureau in writing on blanks furnished by said ——— Bureau.
>
> The reports referred to herein shall be confidential and shall not be open to public inspection.
>
> All persons charged with any duty under this section who shall fail or refuse to comply with the requirements of this section shall be guilty of a misdemeanor and upon conviction thereof be fined not less than $10 nor more than $100 for each offense.

Dr. Allen's committee has pointed out that the proposed bill assures the confidential nature of the reports; information would be given to interested students and physicians according to cases without the use of names.

The recommendations of the special committee of the College, based upon conclusions reached after an independent study, are strikingly similar to those appearing in a report prepared by the New York Cancer Survey Commission several years ago. Said that report:

> An adequate system of reporting cancer would in the course of time make available to the medical profession accurate information, in-

stead of uncertain estimates, on (a) the true magnitude of the cancer problem, (b) the relative incidence of cancer in various sections of the state and among various social and economic groups, (c) the relation between cancer and such factors as occupation, (d) the extent of the alleged increase in cancer above that due to ageing of the population, (e) the accuracy of mortality statistics, (f) the true incidence of the various forms of cancer. In addition there would thereby be furnished an invaluable index as to what sections of the population and what forms of cancer require the greatest attention and application of such control measures as education and the establishment of tumor clinics.

Furthermore, it is reasonable to infer that, as in the case of other diseases which have been studied on a broad group basis, such studies, which would be greatly facilitated by statewide reporting, will discover clues to the nature of cancer which may prove of great importance in its control.

No valid objections to making cancer a reportable disease can now be raised. The disease is fast losing, in the minds of the intelligent public, its former unmentionable character. The majority of patients with cancer at one time or another enter a hospital where the diagnosis and the identity of the patients are not concealed and, in effect, are exposed to considerably greater publicity than could possibly be attributed to confidential reports kept in the closed files of a state department of health. The fact that more than a year ago over 90 per cent of all physicians in three large metropolitan areas (Chicago, Atlanta, and New Orleans) reported by name all cases of cancer known to them during the previous year signifies the willingness of the profession to cooperate in the reporting of cancer.

Copies of the model bill have been distributed to Councilors of the College in the various states by the Commission on Legislation, with the request that they, in collaboration with the proper committee of their state medical societies, seek legislation or official regulation to make cancer a reportable disease. Sponsorship of this public health measure in a disease problem peculiarly within its special province should bring credit to all organized radiology.

CLEVELAND RADIOLOGICAL SOCIETY

At a recent meeting of the Cleveland Radiological Society the following officers were elected for the coming year: *President*, Dr. Harry Hauser; *Vice-President*, Dr. George L. Sackett; *Secretary-Treasurer* (re-elected), Dr. John O. Newton.

NOTICE

A cable from Dr. A. E. Barclay, Oxford, England, states that in an editorial appearing in the June, 1942, issue of the JOURNAL certain erroneous deductions about British radiological services were made from his personal letters. He is transmitting corrections of these impressions which will be published in an early issue of the JOURNAL.

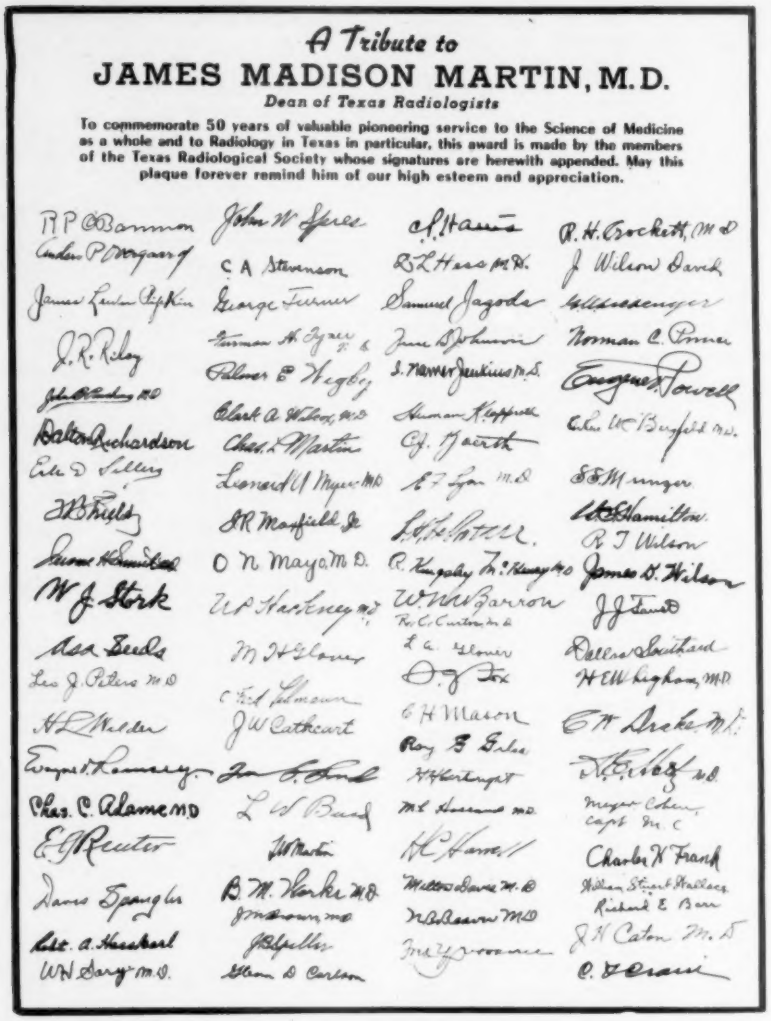
DR. J. M. MARTIN OF DALLAS HONORED BY RADIOLOGISTS OF TEXAS

The *Texas State Journal of Medicine* for July, 1942, page 237, carried the following cut and notice congratulating Dr. J. M. Martin for his many contributions to the science of radiology. This will be of interest to all radiologists.

The Texas Radiological Society at its annual meeting in Houston, February 7, 1942, adopted a resolution expressing appreciation of the radiologists of Texas for the long, outstanding services of Dr. J. M. Martin of Dallas, to the specialty of radiology in the Southwest.

The president, Dr. M. H. Glover, of Wichita Falls, appointed a committee composed of Dr. Davis Spangler, Dallas; Dr. E. V. Powell, Fort Worth, and Dr. Palmer Wigby, of Houston, to prepare a suitable plaque expressing the appreciation of members of the Society for Dr. Martin. The committee secured the signatures of active members of the Society, following which these were made into a bronze plaque, which was presented to Dr. Martin on June 5, 1942, in his room at Baylor Hospital, Dallas, where he had been a patient for several weeks.

The presentation was made by Major Glenn D. Carlson of Fort Sam Houston, with an ap-


A Tribute to
JAMES MADISON MARTIN, M.D.
Dean of Texas Radiologists
To commemorate 50 years of valuable pioneering service to the Science of Medicine as a whole and to Radiology in Texas in particular, this award is made by the members of the Texas Radiological Society whose signatures are herewith appended. May this plaque forever remind him of our high esteem and appreciation.

Bronze plaque of signatures of members of the Texas Radiological Society, expressing their appreciation of the long, outstanding services of Dr. J. M. Martin of Dallas to the specialty of radiology in the Southwest. (Courtesy of the *Texas State Journal of Medicine.*)

propriate expression of appreciation of Dr. Martin on behalf of the Society. These present at the presentation in addition to Major Carlson were Dr. Davis Spangler and Dr. Morton L. Mazer, Dallas; Dr. Palmer Wigby, Houston, and Dr. Tom B. Bond, Fort Worth.

Vol. 48, No. 3

DEPARTMENT OF TECHNIQUE

Department Editor: Robert B. Taft, M.D., B.S., M.A., 105 Rutledge Ave.
Charleston, S. C.

A METHOD FOR THE ROENTGEN MEASUREMENT OF THE LONG BONES*

By O. E. MERRILL, E.E.
BOSTON, MASSACHUSETTS

THE purpose of this paper is to present a simplified and accurate method of roentgen measurement of the extremities. The use of roentgen films for leg measurements has been employed for a number of years, and various methods have been suggested and tried. The two most common among these are first, that in which a lead strip with calibrated perforations is placed on the film at the time of exposure; and second, that in which the extremities are taken on large films which overlap to include the ankles, knees, and hips. Difficulties are encountered in both methods. The technician may not succeed in getting all three joints on the films; improper exposure may fail to show distinct outline of the joint; it is not always easy to position the patient; and finally, there is the item of expense of the large film and the difficulty of setting it up for measurement.

The following method is suggested as a means of overcoming some of the above mentioned difficulties. To aid in positioning the patient, the flat roentgenographic table and Potter-Bucky diaphragm are used together with a specially constructed grid. This grid consists of two pieces of plywood 3/16 inch thick, 18 inches wide by 48 inches long. It is neither expensive nor difficult to make. One of the pieces of plywood is laid out in pencil with lines running across the board, spaced 1 inch apart. Holes are drilled in the board at the ends of the lines, and No. 26 copper wire is drawn tightly through them across the board to cover the pencil lines. Lead numbers are placed on the even-numbered wires (2, 4, and so forth). This surface of the

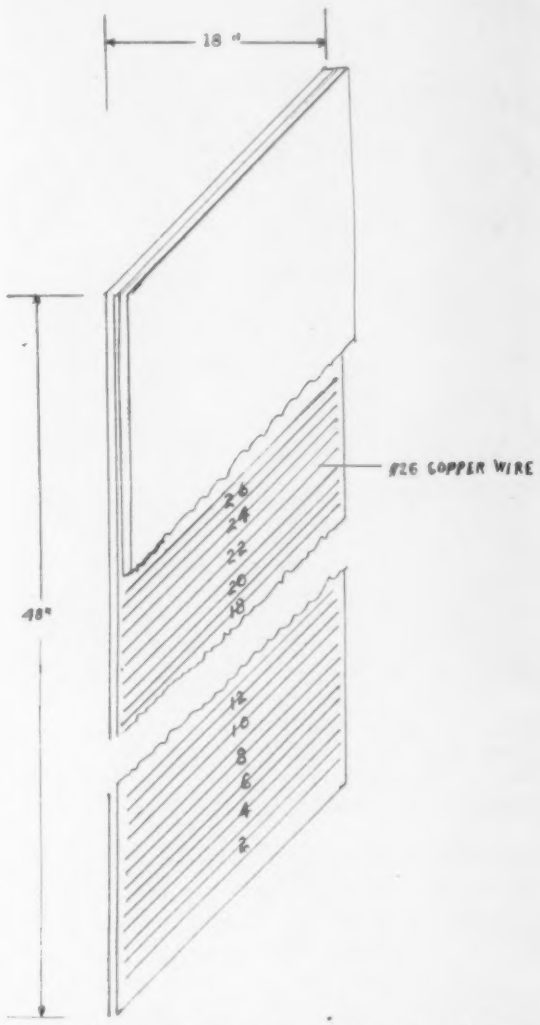


Fig. 1. Sketch of grid showing plywood and placement of wires and lead markers.

* From the Department of Radiology, Massachusetts General Hospital, Boston, Massachusetts.

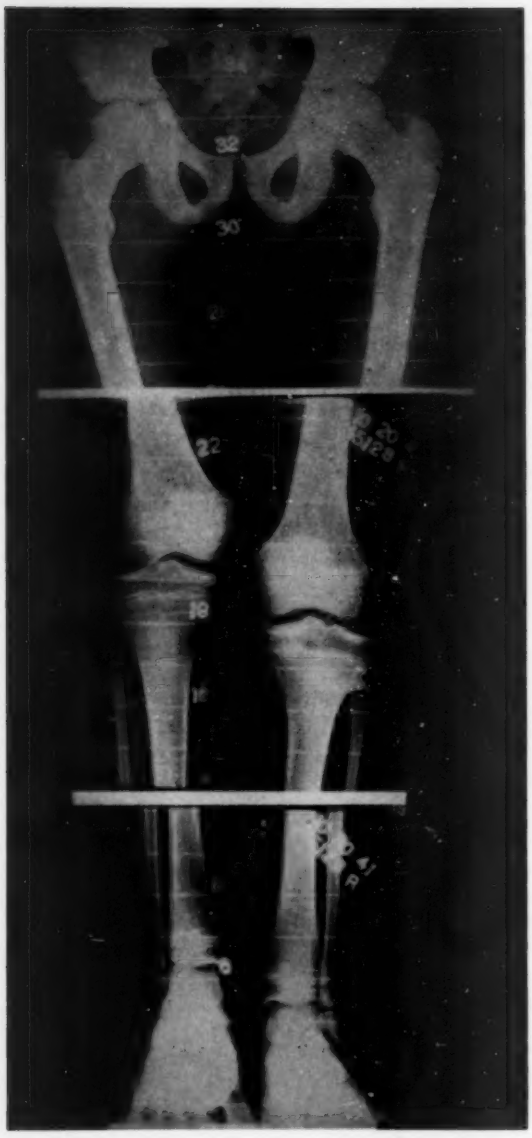


FIG. 2. The three films showing lines and lead numbers from which the direct measurements are made. Note that these films do not include the entire shafts but only a portion about the joints.

board is given a coat of shellac, and the top board is screwed over it.

The procedure for taking the films of the legs is as follows: The patient, in a supine position, is placed on the grid which lies on the table top. The tip of the internal malleolus should be made to fall near the No. 4 lead marker. For accuracy of measurement immobilization is essential and is secured by the use of sandbags at the feet and a strap across the thighs. Three exposures are necessary. The first film taken is an 8 by 10 inch, centered over the ankles; the second a 10 by 12 inch, centered over the knees; the third an 11 by 14, or 14 by 17 inch, over the hips. The centering should be carefully done over the joints to prevent undue distortion. The exposure factors which have been found satisfactory are: 42 inch distance, 100 ma., 48–55 kv.; ankles $\frac{1}{4}$ sec., knees $\frac{1}{2}$ sec., hips 1 sec. Any technique which will give good bone detail may be used. With a tilt table and the proper tube stand films may be taken in the upright position.

The method of measurement from the processed films is as follows: The film of the hips is viewed first and notation is made of the position of the uppermost surfaces of the femoral heads in respect to the lines and lead markers. If the total length of each leg is to be determined, the film of the ankles is used and the relation of the internal malleolus of each ankle and the lines and lead markers are noted. The difference between the readings of each leg gives the length of that extremity. If the points used for measurement fall between the lines, a ruler may be used to determine with reasonable accuracy the fraction of inches. For example, in Figure 2 the left femoral head is at $33\frac{1}{2}$ inches and the left internal malleolus is at 6 inches. The difference in these readings, or the length of the left leg, is $27\frac{1}{2}$ inches. On the right side, the femoral head is at $33\frac{3}{4}$ inches and the internal malleolus at 5 inches, so that the right leg measures $28\frac{3}{4}$ inches.

The advantages of this method are first, the ease of making the films; second, the ease and accuracy of recording the measurements; and third, the economy of films.

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ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

HEAD

FOX, M. S., and BLANKSTEIN, S. S. Skull fractures in children and their sequelae; a critical analysis of 285 cases. *J. Pediat.*, May, 1941, *18*, 629–637.

This study was made to determine the frequency and sequelae of immediate symptoms following skull fractures in children, and the late sequelae. The largest number of cases occurred after the age of four, and were due to traffic accidents; 50 per cent of cases in whom severe shock was present died within forty-eight hours. Unconsciousness was present in 46.6 per cent and stupor in 34.3 per cent. Vomiting occurred in only 21 per cent. Subjective symptoms such as headache, dizziness, tinnitus and visual disturbances were rare. In nearly 50 per cent of cases lacerations, contusions and ecchymosis were present over the fracture site.

Fifteen and eight-tenths per cent of cases had bleeding from the ear. This usually indicates a basal fracture and is of more serious prognostic import. This is equivalent to a compound fracture and the danger of infection is present. Bleeding from the nose and throat was present in 14.4 per cent of cases and was usually due to fracture of the anterior and middle fossae. Extreme fixation and dilatation of the pupils is also of grave prognostic significance. Ecchymosis of the eyelids and subconjunctival hemorrhage is associated with fractures in the anterior and middle fossae in most of the cases.

The present trend is away from spinal punctures, either diagnostic or therapeutic. The trend is also away from other operative procedures such as decompression. Depressed fractures with pressure symptoms, cases with middle meningeal hemorrhage and cases with subdural hemorrhage are operative cases.

In the matter of sequelae headaches were complained of by 30 per cent of cases and in only half of these were the headaches of any severity. Dizziness was present in 8 per cent of cases. The same number complained of a significant disturbance of hearing; 14 per cent gave a history of disturbed intellectual development as shown by retarded school work. The mortality rate in the series of 285 cases was 5 per cent.

Adequate bed rest at the time of the injury and conservative management seem to be of importance in preventing sequelae.—*R. M. Harvey.*

DE BERNARDI, ETTORE. Sull'indagine radiologica della regione sellare in ginecologia. (Roentgen examination of the sellar region in gynecology.) *Radiol. med.*, March, 1941, *28*, 125–140.

The author discusses the general question of the relationship between the hypophysis and genital function and then gives the roentgen findings in several groups of cases, including girls who have not yet menstruated, women who are menstruating regularly, women with excessive and defective menstruation, sterile women and women who have borne children.

He deduces certain rules in regard to the development of the sphenoidal sinuses and sella and the condition of the hypophysis and sexual function. He finds that the parallelism between the development of the sphenoidal sinuses and sexual development is not constant, as the sinuses were highly developed in some girls who had not menstruated and only slightly developed in mature women menstruating regularly. There is no constant parallelism between the morphological type of the individual and the development of the sinuses but there is in general such a relationship and an associated relationship to the type of sexual development.

In cases of metrorrhagia, independently of the constitutional type of the individual, there was marked development of the sphenoidal sinuses and in persons with defective menstruation there was only slight development of the sinuses. The cause of the irregular menstrual type lies in abnormalities of the hypophysis associated with the varying types of development of the sinuses. He concludes that the hypophysis is a regulator of sex function. This is a preliminary report and he advises further study of the subject.—*Audrey G. Morgan.*

Ciarla, Ernesto. Grandi iniezioni peridurali ed epidurali di ossigeno e di aria come nuovo metodo di esplorazione radiologica. Applicazioni terapeutiche. (Large peridural and epidural injections of oxygen and air as a new method of roentgen examination. Therapeutic uses.) *Radiol. med.*, May, 1941, *28*, 247–264.

About five years ago the author began the use of peridural and epidural injection of large amounts of oxygen or air as a means of roentgen examination. At first he used only 100 cc. of air but he has since found that patients can tolerate as much as 500 to 2,000 cc. of either oxygen or air. Air is preferable for practical purposes. The injections can be made epidurally, through the sacrococcygeal membrane, or peridurally through the yellow ligament in the lumbar, dorsal or cervical regions.

The amount of air injected is much larger than the capacity of the epidural space, so it diffuses outward into the loose areolar tissue surrounding the organs of the abdomen, thorax and neck, that between the muscle planes and in the sheaths of the large vessels and the sciatic nerve. Anatomical details of the distribution of the air are given as it is affected by the point of injection, the position of the patient and the resistance encountered.

Roentgenograms are given showing the results of this method of roentgen examination. The organs and structures are outlined by delicate clear stripes due to the presence of air. Good visualization is obtained in this way of the peridural space, the spinal nerves and their branches, the posterior wall of the abdomen and particularly the kidney, the common and external iliac vessels and the femoral vessels, the outlines of the heart, that of the right ventricle being particularly important, the large vessels at the base of the heart, the thoracic aorta, the esophagus, the retrosternal residues of the thymus, the vessel and nerve bundles of the neck and the muscle planes of the neck, back, buttocks and iliac regions.

The reactions produced by these injections are slight and are beneficial rather than otherwise, so that to a certain degree they can be used in treatment. They have a moderate analgesic effect and can be used as a supplement, though not as a substitute for other anesthetics, particularly in spinal segments so high up that the use of true analgesics would be dangerous; this is particularly useful as the air has a tendency to rise to these higher segments. The author has seen these injections relieve neuralgic and arthritic pain, also loss of appetite and general weakness, particularly in cases in which there was a febrile reaction. It is probable that the air acts as a stimulant to the tissues through which it is diffused and produces local and general reactions. He believes the therapeutic use of these injections would be justified in conditions in which there are adhesions around the nerve roots, such as spina bifida occulta and some forms of enuresis and impotence. Another effect when the air is diffused into the carotid region of the neck is slowing of the pulse and lowering of the blood pressure for some days. It is probable that in such cases the pressure of the air stimulates the vagus and the carotid sinus.—*Audrey G. Morgan.*

FRADA, GIOVANNI, and MICALE, GUIDO. Studio clinico-radiologico sulle calcificazioni pineali in gravidanza. (Clinical and roentgen study of pineal calcifications in pregnancy.) *Radiol. med.*, April, 1941, *28*, 209–218.

Small calcium concretions are often found in the pineal gland, even of normal individuals, and about as frequently in males as females. Their frequency increases with increasing age. In a study of the function of the pineal gland during pregnancy the authors made examinations of the gland for the presence of these concretions, choosing 120 women, 40 of whom had never been pregnant, 40 of whom had previously been pregnant and 40 of whom were pregnant at the time of the examination. They chose the women of each group of as nearly the same age as possible so as to eliminate the age factor in the production of the concretions. They found concretions in only 15 per cent of the women who had never been pregnant, in 40 per cent of those who had previously been pregnant and in 41 per cent of those who were pregnant at the time of examination. Evidently pregancy is a factor in producing these concretions. The number of pregnancies does not seem to affect the percentage of positive results. One pregnancy is apparently enough to produce the opacities and in some cases negative at the beginning of the pregnancy they appeared during its course.

The laterolateral projection is best for making these roentgenograms.

There is a functional antagonism between the pineal gland and the prehypophysis. While there is hyperfunction of the prehypophysis during pregnancy there is apparently hypofunction and consequent involution of the pineal gland. This in association with the disturbed calcium metabolism of pregnancy due to the calcium demands of the fetus evidently causes the increased incidence of calcium concretions in the pineal gland during pregnancy.—*Audrey G. Morgan.*

VOISIN, JEAN, and LEPENNETIER, F. Une encéphalocèle orbitaire postérieure. (A case of posterior orbital encephalocele.) *Presse méd.*, Oct. 21, 1941, *49*, 1150–1152.

A case of posterior encephalocele is described in a young girl of twenty-one. She had a pulsatile exophthalmus which had existed, probably, all her life. It could be reduced by slow pressure which caused some pain but no general disturbance and no slowing of the pulse. The roentgenograms of the skull which were taken in different projections are reproduced. Both the lesser and the greater wings of the sphenoid were almost entirely lacking so that the orbit practically had no bony floor and there was no sphenoid fissure. There was a large gap in the frontal bone and the malar was atrophied. The orbit was enlarged in all its diameters, particularly downward by the lowering of its floor to a distance of 7 mm. The embryological origins of these encephaloceles are discussed. Because of the size of the bone defect operation was decided against in this case. Dandy has succeeded in some cases in replacing the floor of the orbit by a subdural bone graft.—*Audrey G. Morgan.*

DE BERNARDI, ETTORE, Sull'aspetto radiografico normale e sulle variazioni patologiche della "cellula" apofisi cristagalli. (The roentgen appearance and pathological changes in the cristagalli process or "cell.") *Radiol. med.*, May, 1941, *28*, 276–286.

The vertical or perpendicular lamina of the ethmoid bone is divided horizontally into two parts by the lamina cribrosa. The upper one of these, because it resembles a cock's comb in shape, is called the cristagalli process. There are three types of this process. In the eburnated type it is made up of compact bone and is represented on the roentgenogram by an opaque line of varying lengths and breadths. The diploic type is fusiform, oval or rounded, has two opaque layers and in the center a spongy structure. The pneumatic type is similar to the diploic except that it has a distinctly pneumatic structure inside the two opaque layers. This type is therefore called the "cell." The first two types are by far the most frequent and are almost equal in number while the pneumatic type is much less frequent. The latter type is, however, much more important from the point of view of pathology.

Because of its position and structure it may become involved in almost all diseases of the nasal and paranasal sinuses. It is often hard to differentiate a cell that has become opacified by disease from an eburnated type that is opaque normally.

The author gives very brief descriptions of several groups of cases in which he made a study of this process, comparing the condition

of the process or cell and that of the sinuses. In some cases both were opacified, in some the cell was opaque and the sinuses clear and in some the sinuses clear and the process opaque. In the latter the inflammation had apparently been localized to or had originated in the cell. He has traced some cases of severe and stubborn headache to inflammation of the cell, which may or may not be accompanied by inflammation of the adjacent sinuses.

He describes 3 cases of epilepsy in which he thinks the disease may have been caused by inflammation of the cell but expects to make a further study of this point and publish his results later.—*Audrey G. Morgan.*

Bignami, Carlo. Studio radiologico dei tumori della mandibola. (Roentgen study of tumors of the mandible.) *Radiol. med.*, March, 1941, *28*, 167–183.

Primary tumors of the mandible include not only the forms of benign and malignant tumor seen in the other bones of the body but also tumors of dental origin. The dental tumors include unilocular cysts, subdivided into follicular and root cysts, adamantinomata and odontomata. Benign tumors of the mandible include fibromata, osteomata, chondromata and giant cell tumors. The malignant tumors that are primary in the mandible are chiefly osteogenetic and osteolytic sarcomata. Melanosarcoma, Ewing's sarcoma and myeloma are rare in the mandible. Brief descriptions and roentgenograms of these various forms of tumors are given.—*Audrey G. Morgan.*

ROENTGEN AND RADIUM THERAPY

La Touche, A. A. D., and Spiers, F. W. Dose measurement in interstitial radium therapy. *Brit. J. Radiol.*, Sept., 1940, *13*, 314–319.

The measurement of gamma rays with condenser ionization chambers was developed by Sievert who showed in how many ways it could be applied in hospital work. This article describes attempts made by the authors during the last three years to apply the condenser method more directly to interstitial treatment. Although this use of it has limitations, which are discussed, in many cases it gives a direct control of the dose while in others it furnishes a check on the dose determined by various methods of calculation.

The condensers, made of elektron or an aluminum alloy, are described and illustrated. They are enclosed in rubber sheaths of thin chromium-plated monel metal tubes. It is best to make the condenser measurements in the operating room with the patient still under anesthesia. Accurate positioning of the condenser is then possible and, as the measurements take little time, the implant can be changed if necessary. Various factors which affect the accuracy of the measurements are discussed.—*Audrey G. Morgan.*

Meredith, W. J. Percentage depth doses in low voltage x-ray therapy. *Brit. J. Radiol.*, Sept., 1940, *13*, 320–321.

A table is given showing the percentage depth doses in unit-density media obtained by different investigators, using a Siemens contact therapy roentgen tube. The figures of the different authors vary by over 50 per cent. A careful analysis made by the author shows that these variations are due to the fact that large amounts of soft secondary radiation are emitted from the sides of the applicator and from the nickel filter at the end of the tube and that the measuring instruments used by the workers give varying measurements for these radiations. Careful measurements with the Siemens ionization chamber showed that the surface dose varied with different factors in the treatment but that the dose at 0.5 cm. and 1 cm. depth were not affected by these factors. Therefore if measurements cannot be made by a standard instrument in all clinics this method of reporting in depth doses should be used.—*Audrey G. Morgan.*

Medical Uses of Radium. Summary of reports from experimental research centers for 1939. Edited by the Joint Radiology Committee of the Medical Research Council and the British Empire Cancer Campaign. *Brit. J. Radiol.*, Jan., 1941, *14*, 1–10.

This is a continuation of a series of reports that have been made by the Medical Research Council for many years. But because of the difficulties in the way of treatment caused by the war this report deals only with experimental work. The subjects dealt with are the production of secondary neutrons as a result of fission of the nuclei of uranium when bombarded by

neutrons, the use of radioactive sulphur as a biological indicator, the Mayneord contour projectors as a means of investigating the distribution of radium throughout a given volume, a study of the effects of radiation on various biological objects, including a study of the variations in biological effect with variations in wave length and a study of the question of whether and to what extent radium can be replaced by radon in clinical treatment.—*Audrey G. Morgan.*

JACOBS, LEWIS G. The evaluation of cancer statistics by correlation analysis. *Radiology*, March, 1941, *36*, 334–342.

The author explains his method of mathematical analysis of the various factors which influence the results in cancer statistics. His method of eliminating the effect of variables, such as the patient's age, the dosage of radiation, the malignancy of the cancer, etc., in comparing the results of different methods of treatment is discussed and illustrated with curves and graphs.—*Audrey G. Morgan.*

GALLAVRESI, LUIGI, and NATALE, PRISCO. Considerazioni statistiche sul valore della röntgenterapia ad alte dosi frazionate (metodo del Coutard) nel trattamento del cancro dell'utero. (Statistics in regard to the value of roentgen therapy by large fractionated doses —Coutard's method—in the treatment of cancer of the uterus.) *Radiol. med.*, April, 1941, *28*, 195–203.

The authors give statistical tables showing the results of their treatment of cancer of the uterus at the National Institute Victor Emanuel III for the Treatment of Tumors in Milan for two different periods, the first from 1928 to 1932 and the second from 1931 to 1934. This has given them time to collect the results for both periods after an interval of five years or more.

The method of treatment was to give first intrauterine treatment with radium followed by roentgen therapy. The radium treatment was practically the same throughout the two periods, but the roentgen treatment during the first period was given by the older methods then in use, while during the second period it was given by Coutard's method of fractionated dosage.

This latter method brought about a great improvement in the five year results. This was true not only in the cases in which no previous treatment had been given but also in the recurrences. In the former group there were 36 per cent cures by the Coutard method as compared with 29.7 per cent cures by the older methods, while in the latter group the Coutard method gave 35.1 per cent cures while the older methods gave only 17.5 per cent.—*Audrey G. Morgan.*

MELVILLE, A. G. G. The double radium mould treatment of carcinoma of the floor of the mouth and lower alveolus. *Brit. J. Radiol.*, Oct., 1940, *13*, 337–344.

Radiotherapy is now acknowledged to be better treatment for tumors of the floor of the mouth than surgery. The author describes and illustrates a double mould method of treatment in use at the Christie Hospital and Holt Radium Institute, Manchester. It is the method of choice in treating cancers of the anterior part of the floor of the mouth and adjoining alveolus. A similar method can be used in treating tumors of the lower lip and cheek.

The tumor is sandwiched between a layer of radium in the mouth and a second one under the chin. These should be parallel or nearly so. The inner mould is a dental compo block carrying radium supported on a baseplate spacer. This is moulded on a plaster cast of the patient's mouth so that it fits exactly. Its thickness is such that the distance between the radium and mucous membrane is 5 mm. The outer mould is carried on a collar moulded on a plaster cast of the patient's neck and lower jaw and the radium container is a rubber tube supported on corks. The corks are cut so that the distance from the outer radium to the skin is 2 cm. When the moulds are in place a roentgenogram shows whether they are parallel and whether the irradiation covers the whole tumor. Generally both moulds are applied ten hours a day for ten days. The dosage now considered optimum is 9,000 r at the mucous membrane and 6,000 r on the skin, and the minimum dose in the irradiated tissue about 5,000 r.

Tables are given showing the details of the results in the 96 cases treated; 47 per cent of the cases were well three years after treatment and 32 per cent well five years after treatment. Another table gives the probable survival rate at three years if gland metastases had not occurred. It shows that 61 per cent might have been expected to remain cured locally at the end of three years.—*Audrey G. Morgan.*

Tod, Margaret C. The optimum dosage in the treatment of carcinoma of the uterine cervix by radiation. *Brit. J. Radiol.*, Jan., 1941, *14*, 23–29.

In a previous paper (*Brit. J. Radiol.*, Dec., 1938) the author described a way of determining the dose in roentgens given to the tissues in the treatment of cancer of the cervix. It was shown that the tolerance dose was determined not by the dose on the surface of the vagina or at the external os but at a point *A* in the paracervical triangle. But this proof that a precalulated dose can be delivered by physical means to point *A* is only a preliminary step to determining the dosage that should be used to give the best results.

In this paper the author analyzes her own 370 cases of cancer of the cervix in an attempt to determine such optimum dosage. She concludes that pending further study the following seem to be optimum dose levels:

7,500 r to 8,500 r in six to seven days, radium only.

8,500 r to 9,500 r for three or four serial weekly applications, radium only.

9,500 r to 10,500 r summated dose at point *A* for combined radium plus roentgen treatment over four to six weeks overall time.—*Audrey G. Morgan.*

Taylor, A. G. C. Supplementary x-ray treatment for carcinoma of the cervix uteri in relation to the direction of the spread of the disease. *Brit. J. Radiol.*, Sept., 1940, *13*, 293–313.

Radium treatment alone of cancer of the cervix can scarcely be developed any further because of the geometrical limitations of this form of treatment. But improvement may be brought about by combining radium and roentgen treatment. By supplementing radium treatment with roentgen treatment a high dosage can be reached if only one side of the pelvis is irradiated. The anatomy of the lymphatics of the pelvis is described and it is shown that the dosage at the wall of the pelvis from radium alone is inadequate.

But an examination of the literature and the author's own cases shows that the disease is confined to the pelvis until a late stage. Inside the pelvis it extends to the parametria and to definite groups of glands lying close together on the wall of the pelvis. Bilateral involvement of the glands occurs in only about 10 per cent of the cases in which the disease has not extended beyond the pelvis. During the radium treatment it is possible to determine the direction and extent of the spread of the disease and in this way work out a scheme for supplementary treatment of the individual case based on the clinical findings. There is often recurrence after radium treatment in or near the cervix. Such recurrences are generally on the side that would be expected from the clinical findings. The author describes the technique of a scheme of irradiation of one side of the pelvis designed to cure such recurrences and any extension of the growth on the side of the primary tumor.

Illustrations are given showing the location of the fields front and back. There are seven small fields through which any desired extent of the cervix may be treated. These fields include the hypogastric glands, the obturator gland and in the intervening space the extrapelvic "principal gland" described by Taussig. There is also a lateral field just above the hip joint directed medially and downwards. Cases illustrating the use of this scheme are described.

An instrument designed to aid in the accurate direction of the roentgen-ray beams is described and illustrated. The histopathology of the tumor need not be considered in deciding on the method of treatment.—*Audrey G. Morgan.*

Anzilotti, A. Eccezionale esito di una Röntgencastrazione per fibromioma. (Unusual result of a roentgen castration for fibromyoma). *Radiol. med.*, April, 1941, *28*, 232–234.

A woman of twenty-five was irradiated for a fibromyoma the size of an adult's head. From January 22 to 27, 1939, she was irradiated over four fields, two anterior and two posterior; a total dose of 1,000 r per field was given at the rate of 200 r per treatment, all four fields being irradiated each time. It was calculated that each ovary was given about 660 r.

The hemorrhage stopped and the fibroma decreased to less than half its original size in the course of six months. From then on there was total amenorrhea until the last of August, 1940. Between September 1 and October 13, there were three hemorrhages, the last so severe that it left the patient almost pulseless. On October 16 she was sent to the hospital where the uterus was found the size of that of a third to fourth month pregnancy. On subtotal hysterectomy

one ovary was found atrophied and reduced to a mass of fibrous tissue while the other was perfectly normal in appearance and showed a recent corpus luteum.

In discussing the possible causes of this failure of roentgen castration the author can only conclude that there must have been a relative radioresistance of the ovary but can assign no cause for it.—*Audrey G. Morgan.*

LEDERMAN, M. Radium treatment of cancer of the penis. *Brit. J. Radiol.*, Dec., 1940, *13*, 393–409.

There is still considerable difference of opinion in regard to the best method of treatment of cancer of the penis. The problem in epithelioma of the penis differs from that in other skin cancers in that the majority of these cancers of the penis are infected and moreover they are keratinizing in type and therefore radioresistant, the skin and mucous membrane of the prepuce are more sensitive to irradiation than other areas and lymph node metastases are common and quite generally bilateral. But Desaive in an analysis of results up to 1933 found one year survival in 57.6 per cent of the cases treated by radiotherapy alone, 53.9 per cent in combined radiotherapy and surgery, and 34.4 per cent in surgery alone. Hansson in a review of the material treated at the Radiumhemmet from 1912–1937 gives a five year survival rate of 85 per cent for Stage I, 58 per cent for Stage II, none for Stage III and 65 per cent when all three groups are considered together. The author discusses the technique used in his own work at the Royal Cancer Hospital, London. Up to 1936 they used a moulded applicator in most cases. Since then they have used teleradium treatment, irradiating the glans and the greater part of the shaft of the penis homogeneously from a distance of 5 to 6 cm. The regional lymphatics are adequately treated whether there are palpable nodes or not. The teleradium units used for this treatment are described and illustrated. The treatment is fractionated. Graphs are given showing the amount and rate of administration of dosage both to the primary tumor and the lymphatics, the response of the skin, primary tumor and lymph nodes to the treatment and the changes in the blood count and weight as an index to the effect of treatment on the general condition. A table is given showing the details of treatment and results in 28 cases, 14 of them with the radium applicator, 10 by teleradium and 4 by implantation. The results for the whole number of cases treated by all methods were 53.8 per cent five year cures and 61.9 per cent three year cures.—*Audrey G. Morgan.*

SCHENCK, SAMUEL GEORGE. The management of cancer of the breast with pre-operative and post-operative irradiation. *Radiology*, March, 1941, *36*, 315–323.

There are probably about 50,000 women with cancer of the breast in this country at the present time. With the treatment in use ten to fifteen years ago only about 20 per cent of them could have been saved but with present treatment about 40 to 50 per cent can be cured. The improvement lies in the use of radiotherapy. Preoperative roentgen treatment should be used in all cases as soon as the diagnosis is made. Cross-fire treatment through several fields with small, daily, highly filtered doses should be given according to Coutard's method. The dosage and the details of treatment must be varied to suit the individual case but in general about 2,000 to 2,600 r should be given to each breast field and about 1,600 to 2,000 r to the axillary fields. This treatment is completed in twenty-seven to thirty-three days and about eight weeks later radical operation should be performed. In from four to six weeks after operation another series of high-voltage treatments is given. This is similar to the preoperative treatments except that the dosage is lower. If in spite of this there are local recurrences additional treatment may be given cautiously.

Artificial sterilization should be brought about in patients who are still menstruating as the ovarian hormones stimulate the gland tissue in the breast.—*Audrey G. Morgan.*

RUBENFELD, SIDNEY, and SCOTT, L. D. X-ray treatment of leukemias. *Radiology*, March, 1941, *36*, 352–355.

The authors discuss 117 cases of leukemia treated in the Radiation Therapy Service at Bellevue Hospital from 1925 to 1938. Of these 58 were of the lymphogenous type, 58 of the myeloid and 1 of the monocytic form. The disease is much more frequent in males than females, the proportion being 6 to 1 in lymphatic leukemia and 2 to 1 in the myeloid form.

These patients respond well to irradiation at first. The white count falls rapidly and continues to do so after treatment has stopped. There-

fore treatment should be discontinued when the count has reached 50,000 to 75,000. If anemia occurs it should be treated with transfusions and iron. The general condition of the patient is more important in judging results than the white cell count. A patient with 75,000 to 100,000 white cells may show no symptoms. Such a patient should not be treated for it is well to postpone as long as possible the refractory stage that invariably at some time follows the beginning improvement.

The results in these cases were the same as those previously reported. There were no cures but the patients were kept alive for from three to six years. They also had intervals when they could go on with their ordinary work. This is the great value of roentgen treatment in leukemia.—*Audrey G. Morgan.*

MISCELLANEOUS

Gray, L. H. Physical investigation of the contribution of the photo-electrons from sulphur to x-ray ionisation. *Brit. J. Radiol.*, Jan., 1940, *13*, 25–30.

In the presence of elements of a high atomic number, such as sulphur and calcium, photo-electric emission brings about an increase in the energy per unit volume of tissue exposed to roentgen irradiation. In this article an ionization chamber is described and illustrated which is designed to measure the fractional increase of energy due to such photo-electrons from sulphur.

Measurements were made with mouse skin containing keratin layers rich in sulphur which was cemented to pieces of graphite used to form the top and bottom of the chamber and others using as top and bottom of the chamber layers of graphite covered with a layer of sulphur about 0.3 mm. thick. Curves and tables are given showing the details of the results. From these it is evident that when a cell is separated from pure sulphur by a layer of tissue 14μ thick there is the same increase of energy per unit volume with equal doses in roentgens of roentgen rays of 117 and 190 kv., but that this increment of energy is about 100 per cent greater than that yielded by the same number of roentgens of radium irradiation. That is, the same reaction is brought about by two qualities of roentgen rays but that this is much greater than the reaction brought about by an equal dose of radium rays. However the photo-electric emission from the sulphur did not seem to account for more than about a third of this difference. It is hoped to obtain further data which will give a more complete explanation of these observations.—*Audrey G. Morgan.*

Gray, L. H., Read, John, and Wyatt, J. G. A neutron generator for biological research. *Brit. J. Radiol.*, March, 1940, *13*, 82–94.

A neutron generator to be used in biological research is described and illustrated. It was believed that neutrons might prove useful in treating cancer and so the British Empire Cancer Campaign agreed to finance a research on the biological action of neutron rays at the Mount Vernon Hospital and Radium Institute, Northwood, Middlesex. Construction of the apparatus began Jan. 1, 1936, and the first biological experiments were done in March, 1938. A 400 kilovolt Cockcroft and Walton circuit is used and an ion tube with a low voltage arc ion source. The disintegration of deuterium by deuterons promised to give the greatest yield of neutrons at this voltage, and this reaction has the great advantage of being free from associated gamma rays which might complicate the interpretation of the biological results. A film of deuterium paraffin-wax on copper, cooled by running tap water, is used as the target. The materials and apparatus cost 600 pounds sterling, the shed to house it 150 pounds and maintenance since that time has cost 80 pounds per year. Two physicists and a mechanic spent two years in the building and improvement of the generator.—*Audrey G. Morgan.*

Snell, George D. Induction by roentgen rays of hereditary changes in mice. *Radiology*, Feb., 1941, *36*, 189–196.

Male mice were irradiated with 600 to 800 r and mated to normal, non-irradiated females. There was a fertile period of about two weeks in the males, followed by a sterile period of about three months and then a return of fertility. But certain of the irradiated animals produce small litters, a condition known as semi-sterility. This is brought about not by gene mutations but by chromosome mutations, that is the loss of whole segments of chromosomes or their transfer to other chromosomes. This translocation results in the production of offspring apparently normal but semi-sterile. Half of the offspring of a given animal are normal and half semi-sterile. In addition, some of the embryos will die as the result of the loss of a chromosome segment.

Females irradiated with 600 to 800 r became completely sterile. When irradiated with 240 to 280 r 6 per cent of the offspring were genetically abnormal. This was a smaller percentage than in the male but the dose was also less. Males irradiated with neutrons showed the same effects as when irradiated with roentgen rays.

In the discussion the application of these results to human beings was considered. The results in mice did not show until the second generation and it is probable that few examinations have been made of the grandchildren of irradiated persons. The question was asked whether irradiation of immature germ cells killed them so that no offspring were produced and therefore no abnormalities. Dr. Snell replied that in his mice offspring produced in the second fertile period showed little evidence of translocation. As applied to human beings, he thinks this indicates that if a considerable time passed between the irradiation and the conception of children there was less chance of abnormality than if conception took place very soon after irradiation.—*Audrey G. Morgan.*

MOTTRAM, J. C., and GRAY, L. H. The relative response of the skin of mice to x-radiation and gamma radiation. *Brit. J. Radiol.*, Jan., 1940, *13*, 31–34.

Experiments on white mice are described in which short lengths of the tails were irradiated, in some cases with roentgen radiation and in others with gamma radiation. The dose given was the same at all points throughout the irradiated part of the tails. Of the 111 animals irradiated 47 were treated with gamma radiation, 41 with 190 kv. roentgen rays and 23 with 117 kv. roentgen rays. To get a complete range of reactions it was found necessary to give from 2,500 to 7,000 r of roentgen rays and from 4,000 to 8,000 r of gamma radiation. The reactions tested were erythema, desquamation, epilation and exudation. For the production of all of these changes it required larger doses of gamma radiation than of roentgen radiation. Charts are given showing the results graphically. The ratio of effectiveness for roentgen and gamma irradiation was 1.3 for erythema and desquamation and 1.6 for epilation and exudation.

The duration of irradiation was kept the same in all cases so that the results were not affected by variations in the time factor.

Though the dose was the same for the different types of radiation, the amounts of energy released by roentgen and gamma irradiation were not necessarily the same. An addition to the energy produced by roentgen irradiation was furnished by photo-electric emission from elements of high atomic number, such as sulphur and calcium. Sulphur is present in the keratin of the skin and calcium in the bones of the tail. Though the differences found in roentgen and gamma radiation could not be accounted for completely by mathematical calculation from the data furnished by the experiments it is evident that photo-electric absorption explains, at least in part, the differences that are seen biologically. The differences are evidently not caused by wave length except to the extent that wave length may determine the amount of energy released in the cell by the process of photo-electric absorption.—*Audrey G. Morgan.*

SCHONS, EDWARD. Importance of accurate collimation of the beam in deep roentgen therapy; effect of the size of the focal area and position of the limiting diaphragm, with special reference to supervoltage. *Radiology*, Feb., 1941, *36*, 154–158.

In deep roentgen treatment it is extremely important to limit the irradiation to the area to be treated in order not to injure normal tissue. The boundaries of the tumor or lesion to be treated should be determined as accurately as possible and then the beam so limited that it will affect only the lesion and a safe zone around it. This can be done by using lead cones of the proper size for each area treated of sufficient thickness to protect from rays of the voltage used. Thick lead diaphragms at a distance from the field are not reliable. The cones should be placed as near the area to be treated as possible. This limits the penumbra or fuzzy zone of irradiation of decreasing intensity around the focal area. This is ordinarily taken care of by the usual types of diaphragming with 200 kv. radiation but with supervoltage, even though the beam is more sharply defined in the tissues because there is less backscatter, this advantage is apt to be lost by incorrect diaphragming. Diagrams illustrating the application of the principle are given.—*Audrey G. Morgan.*

JONES, D. E. A. The determination from absorption data of the distribution of x-ray intensity in the continuous x-ray spectrum. *Brit. J. Radiol.*, March, 1940, *13*, 95–101.

The quality of the roentgen-ray beam is defined by the wave length of the radiation. While a simple statement of the wave length completely defines the quality for a monochromatic beam, the definition is much more complex for a heterogeneous beam, as it requires a knowledge of the relative intensity of every component wave length in the beam. Of course this information may be obtained by roentgen-ray spectrometry but this is far too involved to be used practically in roentgen treatment.

Silberstein suggested the following equation, $I_x = I_0 e^{-Ax - B\sqrt{x}}$ to represent the transmission curve for a heterogeneous beam of roentgen rays, the original intensity of which was I_0 after its passage through a thickness x of absorbing material. A and B are constants.

Silberstein, however, applied his results only to beams of 100 kv. or less. A critical discussion of the equation is given and it is found not entirely reliable for beams in the region used for deep therapy. A much better agreement between the experimental and empirical data can be obtained by including a constant d in the equation, so that the exponent becomes $-Ax - B(\sqrt{x+d} - \sqrt{d})$. The method of calculating the constants A, B and d is described and it is shown how the spectral distribution of dosage rate in the heterogeneous roentgen-ray beam can be calculated without the use of spectrometric analysis. This method is of special value in the range of rays used for deep roentgen treatment.—*Audrey G. Morgan.*

Eddy, C. E. A note on clinical dosemeters. *Brit. J. Radiol.*, April, 1940, *13*, 130–135.

With progress in radiation therapy it has become the general practice to determine the skin, healthy tissue and tumor doses given to each individual patient. This is not particularly difficult with radium, but in roentgen treatment the intensity and quality of the radiation varies with so many factors that measurement becomes very difficult. Frequently dosage calculations are derived from measurements made on the roentgen-ray beams in hospitals, using some form of clinical dosemeter. The limitations of such dosemeters are discussed. Clinical dosemeters can be used to measure dosage only after comparison with a free air chamber and even then the measurements are valid only for those qualities of roentgen rays for which such a comparison has been made.

The author, who is physicist in charge of the Commonwealth X-ray and Radium Laboratory of the University of Melbourne, describes the method of calibration of clinical dosemeters in use in Australia. The Commonwealth Laboratory maintains a standard by which the state and local dosemeters are calibrated. The difficulties encountered in calibrating all Australian hospital dosemeters are discussed but the conclusion is reached that regularly calibrated clinical dosemeters can be used to measure free air dosage rates and roentgen-ray quality with the necessary degree of accuracy. Calibration and inspection at regular intervals and particularly following any replacement of a part or any departure from constant behavior keeps up the desired standard. Though many dosemeters have been tested it has been impossible to decide upon any one that is superior to the others. Reliability of performance depends on the care given the instrument rather than on the make. Immobilization of the measuring instrument is important. Recent models provide for permanent wall mounting rather than table mounting.

The methods heretofore in use for checking the amount of radiation received by personnel in roentgen and radium departments have had the disadvantage of measuring only the total exposure over a period of several hours. The amount of scattered radiation at any given point from a single exposure can be measured by large ionization chambers of about 3 liters volume fitted to almost any form of clinical dosemeter.—*Audrey G. Morgan.*

Lamerton, L. F. A physical investigation of the radiation from a low-voltage x-ray tube (cautery technique). *Brit. J. Radiol.*, April, 1940, *13*, 136–146.

Low voltage roentgen treatment has been so successful that there has been a demand for an apparatus that can be used in body cavities and that can give a high surface dosage rate so that the treatment time may be short. This has been met by the Philips Metalix apparatus for contact and cavity treatment. This apparatus is described and a study made of the physical properties of the radiation produced by it at 44 kv., 2 ma. Absorption measurements for filtered and unfiltered radiation were made in aluminum, water and certain solutions. The first half-value layer of unfiltered radiation was found to be 0.30 mm. aluminum, corresponding to an equivalent wave length of 840 X.U. Cen-

tral axis depth dose curves for filtered and unfiltered radiation at various focal-skin distance are given and also complete isodose curves. A condenser chamber for the measurement of the dosage rate in air which may be used with a standard Victoreen condenser dosemeter is described. A surface dosage rate of 7,610 r/min. is obtained with unfiltered radiation at the shortest focal-skin distance (2.0 cm.) but penetration is very slight, as 4 mm. water is sufficient to reduce the dosage rate to one-half its surface value. Absorption by the water was so great that the amount of scattered radiation outside the geometrical edge of the beam was small.

The methods of measuring the stray radiation around the tube are described. van der Plaats and den Hoed have described physical measurements made with the Philips Metalix apparatus. There are some divergences between their depth doses and those obtained by the author, probably due to differences in the design of the ionization chamber used.

A description is given of an attempt to determine the energy distribution in the spectrum of the radiation by an analysis of the absorption curve in aluminum by Silberstein's method.—*Audrey G. Morgan.*

KAYE, G. W. C., and BINKS, W. The emission and transmission of X and gamma radiation. *Brit. J. Radiol.*, June, 1940, *13*, 193–212.

This paper deals with the rates of emission of roentgen radiation from present-day roentgen tubes, excited at various voltages, particularly very high voltages and gamma radiation from radium sources. As the authors had experimental facilities available at the National Physical Laboratory, Teddington, Middlesex, only up to about 400 kv., they surveyed recent data from sixteen other research centers in various countries so that they have figures for all voltages from 200 kv. to about 2,000 kv. Tables are given showing the details of such data. From these it is evident that the roentgen-ray output of a tube in roentgens is predictable at practically any voltage under standard conditions of operation, whether for "reflection" or "transmission" roentgen-ray targets. They also show that the maximum roentgen-ray output from a present-day 2 million volt tube is comparable to the gamma-ray output from about 16,000 grams of radium.

This is followed by a discussion of a method of calculating the progressive absorption of roentgen rays by materials, based on Kramers' formula for roentgen-ray emission. Graphs are given for a graphical method of solution, making use of theoretical data for the components of the absorption coefficients of a "narrow" beam of roentgen-rays at a series of selected wave lengths in the continuous spectrum. The derived transmission curves for different voltages are illustrated by lead filtration, particularly as applied to securing adequate protection for roentgen ray workers, on the basis of the accepted tolerance dosage rate of 10^{-5} r/sec. The good agreement between the calculated lead protection rates and experimental observations published elsewhere for voltages up to 1 million, suggests the possibility of forecasting the degree of lead protection required for even higher voltages.

A somewhat similar method is followed for a narrow beam of gamma rays from radium B and C, using published data for the energy distribution and absorption coefficients of the several components of the line spectrum of the rays. The calculated transmission curve, which in this case, too, agrees well with experimental observations carried out at the Laboratory, corresponds to a roentgen-ray beam excited by about 3,000 kv.

In a similar way the "lead equivalents" of various materials can be calculated for a wide range of roentgen-ray voltages. The method is illustrated by the lead-equivalent curve of a barium sulphate concrete, which, in common with that of other protective materials, increases with voltage to a maximum at about 90 kv., followed by a minimum at 200–300 kv., rising steadily after that to very high voltages. Experimental observations with 50 to 400 kv. roentgen rays agree satisfactorily with these computed curves and seem to justify calculations for higher voltages. Gamma-ray measurements also agree with calculations, the results finding a place on the roentgen-ray lead-equivalent curves at between 3,000 and 4,500 kv., depending on the thickness of the specimen.—*Audrey G. Morgan.*

THORAEUS, R. A small ionisation chamber able to serve as a portable substitute for a standard chamber. *Acta radiol.*, 1941, *22*, 260–267.

The author describes and illustrates a small ionization chamber that is independent of wave length through so large a range of qualities of radiation that it can be used as a portable sub-

stitute for a standard chamber if provided with a good reading unit. Of course a portable secondary standard cannot give the same degree of accuracy as a standard chamber, but with the chamber here described the margin of error is not more than ±2, which is sufficiently accurate for ordinary purposes.—*Audrey G. Morgan.*

Miller, Henry. A reflecting screen facilitating the removal of foreign bodies and positioning in radiography. *Brit. J. Radiol.*, Feb., 1941, *14*, 77–78.

In removing foreign bodies under the fluorescent screen one of the difficulties is to manipulate surgical instruments with any degree of accuracy because of the overlying screen. Here a reflecting screen is described and illustrated which entirely overcomes this difficulty. A plumb-bob, the shadow of which is superimposed on that of the foreign body, aids in localization. The device is very simple and consists of an inverted Levy-West fluorescent screen below which a mirror is placed, set at a slight angle which can be adjusted. The photograph and drawing which are given explain the use of the apparatus.—*Audrey G. Morgan.*

Chaussé, Clément. The localisation and extraction of radio-opaque objects by means of the "light compasses." *Brit. J. Radiol.*, Aug., 1940, *13*, 257–266.

When a foreign body is embedded in a mass of tissue such as muscle or brain "geometrical localization" must be used. The author describes his method of geometrical localization by means of "light-compasses," derived from his first apparatus, previously described and known as a stereoroentgenographic centering apparatus. An illustration of the present apparatus is given and its method of use described. The centering apparatus has been improved by the addition of two new light-sources, an operating table and a camera with a fluoroscope. Its advantages over Hirtz's compasses are discussed, among them being that the technique of its use is simpler and does not require a drawing. With the light-compasses the construction in space is done automatically by maneuvering the knobs controlling the movements of the tube, ball and socket joint (film or camera-fluoroscope) and target-finder; it is almost impossible to make an error.

Roentgenograms illustrating the use of the compasses are given.—*Audrey G. Morgan.*

Attilj, Sordello. Sulla schermografia. (Fluorography.) *Radiol. med.*, April, 1941, *28*, 224–227.

Fluorography or screen photography consists in making with a camera of the Leica type a photograph of the fluorescent screen exposed for a short time at great intensity and moderate tension. The photographs are made on films 2.4 by 2.4.

By this method a large number of examinations can be made in a short time at a very low cost and it has therefore been recommended especially for mass examinations for tuberculosis. But from his experience in making these fluorograms of a large number of soldiers the author does not believe that the method is capable of showing beginning tuberculosis. Because of its cheapness and rapidity it can be used with advantage in demonstrating larger tuberculous lesions, 2 to 3 mm. in diameter, in the control of pneumothorax and in demonstrating bone and heart lesions.—*Audrey G. Morgan.*

Gray, E. D. A simple method for the use of standard stereoscopic radiographs in plane differentiation. *Brit. J. Radiol.*, Oct., 1940, *13*, 354–355.

Generally the stereoscopic roentgenogram shows only a three-dimensional image. But the author describes a method by means of which clear images of successive planes may be obtained. This is done by superimposing two stereoscopic films with the tube side toward the observer and then sliding one film on the other in directions corresponding to the directions of the tube shifts. The method is illustrated by a description of its application in bringing out calcifications in the choroid plexuses and pineal body. He has found it especially useful in work on the skull, particularly in determining the side on which fracture has occurred when the fracture is visible only in a lateral view and in differentiating local bone condensations in the skull from intracranial calcifications. It has also shown the lateral displacement of a faintly calcified pineal body which could not be seen in anteroposterior views.—*Audrey G. Morgan.*

Jones, H. B., Chaikoff, I. L., and Lawrence, John H. Phosphorus metabolism of the soft tissues of the normal mouse as indicated by radioactive phosphorus. *Am. J. Cancer*, Oct., 1940, *40*, 235–242.

Experiments are described in which the phos-

phorus metabolism of the soft tissues was studied by giving normal mice intraperitoneal injections of 0.2 cc. of an isotonic solution of radioactive sodium phosphate (Na_2HPO_4) which contained 3 mg. phosphorus per cubic centimeter. The amount injected contained 5 microcuries radioactivity determined by a uranium standard. The animals were killed after varying periods up to seventy-three hours, and the phosphorus content of liver, kidneys, small intestine, blood, lymph nodes, lung, skeletal and heart muscle and brain determined.

The technique for determining the radioactivity of the retained phosphorus is described and graphs given showing the amount of labeled phosphorus contained in the various tissues after varying intervals. All the tissues except brain showed a sharp rise in phosphorus concentration for from five to ten hours. The brain showed an increase for a much longer time. The maximum concentration was not reached until the twenty-fourth hour and it remained at that level until the end of the seventy-three hour period, while the other tissues showed a progressive loss after reaching the maximum.

The most active metabolism, based on the rate at which labeled phosphorus was deposited and removed per gram of tissue, was shown by the liver, small intestine and kidney, followed by heart and skeletal muscle, lymph nodes and lungs. Blood and brain showed the lowest rate. At the end of eight hours after the injections about 90 per cent of all the phosphorus deposited was contained in the liver, small intestine and muscle.

The figures obtained serve for comparison with previous studies of phosphorus metabolism in tumor tissue.—*Audrey G. Morgan.*

JONES, H. B., CHAIKOFF, I. L., and LAWRENCE, JOHN H. Phosphorus metabolism of neoplastic tissues (mammary carcinoma, lymphoma, lymphosarcoma) as indicated by radioactive phosphorus. *Am. J. Cancer*, Oct., 1940, *40*, 243–250.

Phosphorus metabolism was determined in three types of tumor, carcinoma of the breast, lymphoma and lymphosarcoma, by injecting the radioactive isotope of phosphorus into mice with these types of tumor. The experimental methods are described and graphs given showing phosphorus activity in these types of tumor as compared with that of normal tissue. A comparison between the different types of tumor was also made by inoculating the same animal at the same time with the different types.

All these types of tumor take up phosphorus rapidly soon after it is injected. In this respect they resemble the most active of the normal tissues, liver, kidney and small intestine, but, unlike the normal tissues, they show a capacity for retaining the phosphorus for a long time.

The phosphorus activity was similar in the three types of tumor. The rate of deposition of total labeled phosphorus was the same in the lymphoma and lymphosarcoma, though the phospholipid activity of lymphosarcoma is at least twice as great as that of lymphoma. The phosphorus activity of both lymphoma and lymphosarcoma was at least twice as great as that of normal lymph nodes.

Lymphosarcoma grew much more rapidly than breast cancer and lymphoma, though their phosphorus activity was about the same. This does not necessarily mean that there is no relation between phosphorus activity and rate of growth, as mere increase in size is not an index of mitotic activity and cell degeneration. In fact, it has been suggested recently that the high uptake of radiophosphorus by tumor nuclei is a function of mitotic activity.—*Audrey G. Morgan.*

MA, W. C., and HSÜ, CHIEN-LIANG. The effect of roentgen radiation on spinal ganglia of albino rats. *Am. J. Cancer*, Nov., 1940, *40*, 335–342.

Normal albino rats were treated with varying doses of roentgen radiation administered in some cases directly over the spinal ganglia and in others to the legs. On the second day after the completion of the irradiation the spinal ganglia were removed and examined with special staining methods. Photomicrographs of the histological findings are given.

Whether irradiated directly or indirectly it was found that the functional activity of the ganglia was disturbed by the irradiation, and that the degree of disturbance was proportional to the size of the dose. Small doses may cause hyperactivity of ganglion cells, as shown by increase of the mitochondria, indicating an attempt at repair, while larger doses cause hypoactivity, showing failure of the attempt at repair.

The changes seen were as follows: the outline of the cells was normal or irregular or showed decided shrinkage; the nuclei were small, irregu-

lar, elongated or indistinct in outline; the mitochondria were increased or decreased in number and were granular and poorly stained. The Nissl substance became invisible as dosage was increased. The Golgi apparatus was decreased in amount and changed from a network to segments or droplets and in some cases became a localized mass instead of being evenly distributed. Droplet formation in the mitochondria brought about a picture similar to that seen in fowls with beriberi, and the appearance of many cells resembled that of the cells in animals suffering from vitamin deficiency. The injury caused by the rays evidently brings about deficient nutrition.—*Audrey G. Morgan.*

Gernez-Rieux, Ch., Driessens, J., Bizard, G., and Breton, A. Nouvelles recherches sur les lésions pulmonaires expérimentales secondaires aux sections ou excitations vago-sympathiques. (Study of the experimental pulmonary lesions following section or stimulation of the vagus and sympathetic nerves.) *Presse méd.*, Oct. 21, 1941, *49*, 1132–1135.

The vagus and sympathetic nerves were sectioned or stimulated by electricity in dogs and cats and histopathological and roentgen studies made of the results. The results seen after section were about the same as those after electrical stimulation. They were about the same after manipulation of the vagus and the sympathetic and the histopathological lesions were about the same after unilateral and bilateral manipulation. The histopathological picture showed both cellular and exudative changes very irregularly distributed, the picture resembling that of a bronchopneumonia.

The roentgen picture after the manipulation of the two nerves was about the same, but there was no change on unilateral manipulation; after bilateral lesions the change appeared generally only on one side and consisted of a uniform and not very dense opacification of the lung field, resembling that of acute edema of the lung. The change did not start until the beginning, or sometimes near the end, of the fifth hour after the lesions. It persisted on an average about ten hours and then disappeared gradually until the lung field appeared normal. The roentgen images did not correspond to the histological changes for they were always homogeneous even when the microscope showed polymorphous diffuse lesions.

The changes produced by lesions of the nerves ran the whole gamut of those seen in acute lung diseases.—*Audrey G. Morgan.*

Lasnitzki, Ilse. The effect of x-rays on cells cultivated *in vitro*. *Brit. J. Radiol.*, Aug., 1940, *13*, 279–284.

The work described here is part of an investigation being carried on by the Strangeways Research Laboratory, Cambridge, into the biological response of normal and malignant tissues to different wave lengths of roentgen radiation. The material used for these examinations was the choroid and sclerotic of chick embryos nine to eleven days old. The radiation was from a hot cathode roentgen tube operating at 160 kv. constant potential, 8 ma., 0.7 mm. copper and 1.2 mm. aluminum filter. The half-value layer was 1 mm. copper corresponding to an effective wave length of 0.150 Å. The intensity was 29 r/min. and the cultures were exposed for 200 seconds, that is the dose was 96.7 r. After irradiation the cultures were returned to the incubator for from twenty minutes to twenty-four hours and then fixed and stained for histological examination. The changes found over the twenty-four hour period are described.

At first there was a decrease of mitosis to 23 per cent of the normal count. After that there was an attempt at recovery of mitosis accompanied by the appearance of degenerated cells. Throughout the period of observation the presence of degenerated cells could be accounted for by a cellular breakdown occurring at the end of prophase.

There is a striking similarity between these results and those found on irradiating cells in vivo. Evidently, therefore, the degeneration produced by irradiation in these experiments is independent of any effect produced through the blood circulation.—*Audrey G. Morgan.*

Lorenz, K. P., and Henshaw, P. S. Radiobiologic action and the killing effects of x-rays on Achromobacter fischeri. *Radiology*, April, 1941, *36*, 471–481.

The history of the study of the action of roentgen rays on various biological objects is reviewed. Experimental work on *Achromobacter fischeri* is then described; this is a motile free-swimming sea vibrio which has certain definite advantages over other organisms as a test object. A table is given showing the results of irradiation for different times with different dosages and a semi-logarithmic plot showing the

percentage of bacteria that survive after exposure to 200 kv. roentgen rays. The survival curve is found to be of the exponential type which places *Achromobacter fischeri* in the single-hit-to-kill class of Blau and Altenburger. This is the simplest type of reaction in which only a single hit is required to cause death of the cell.—*Audrey G. Morgan.*

CAMERON, JOHN A. Recovery of carbon monoxide poisoned monkeys under x-ray treatment. *Radiology*, April, 1941, *36*, 486–487.

Monkeys were kept for five to eight and one-half minutes in 12.5 per cent CO and then irradiated with a Victor roentgen machine that delivered 130 r per minute; 140 kv. (peak), tube current 4 ma.; target distance 10 inches.

The protocols of the experiments are given. The conclusion is reached that roentgen treatment in moderate amounts was a critical factor in the recovery of the 7 cases reported.—*Audrey G. Morgan.*

MATHEY-CORNAT, R. Contribution a la radiobiologie du tissu osseux: Applications thérapeutiques. (Radiobiology of bone tissue and its therapeutic applications.) *Presse méd.*, Aug. 6–9, 1941, *49*, 863–865.

The author discusses the roentgen study of bone at its different stages of development, analytical roentgenography by the methods of planigraphy, tomography and biotomy and the historoentgenography of Lamarque, which is a sort of cytochemical analysis by means of very soft roentgen rays which it is hoped will lead to a better understanding of the factors which influence the radiosensitiveness of tissues. A study has also been made by radiobiological methods of the metabolism of calcium and phosphorus in the skeleton as a whole and the production of phosphate in the bones of irradiated animals. Experiment has shown that the metabolism of calcium and phosphorus is stimulated by irradiation with both soft and hard roentgen rays.

Such methods of radiobiological study are quite recent but it is hoped that their application will prove of value in the working out of radiation methods of treatment of pathological conditions in bone.—*Audrey G. Morgan.*

SPEAR, F. G., and GLÜCKSMANN, A. The effect of gamma radiation on cells *in vivo*. Part III. Spaced radiation. *Brit. J. Radiol.*, Feb., 1941, *14*, 65–76.

This article represents a continuation of work described in previous papers on the effect of gamma radiation on the normal brain and eye of the frog tadpole. In the experiments described in this paper tadpoles were exposed to a dose of 536 r gamma rays delivered in six different ways with the object of determining whether the amount of degeneration seen after exposure could be increased by delivering the second of two exposures at the moment when mitosis was least active as a result of the first exposure. The technique is described and graphs given showing the details of the results. The conclusion is reached that in multiple exposures to equal doses to obtain the maximum effect on any given tissue, as the dose is increased the interval between the two exposures should be increased.—*Audrey G. Morgan.*

WARBURTON, F. L. The influence of radiation on the electrolytic coagulation of mastic sols. *Brit. J. Radiol.*, Jan., 1941, *14*, 30–35.

It has long been known that certain colloids could be coagulated by irradiating them, but a dose of several thousand roentgens was required. But it seemed probable that smaller doses might sensitize sols toward electrolytic coagulation in much the same way as photographic emulsions are sensitized to reduction by chemicals.

In this article experiments are described in which the mastic sol was mixed in definite proportion with a sodium chloride solution of definite strength and the time required for the sol to coagulate was taken as a measure of the effect of the radiation. Radon and ultraviolet radiation was used. The results are shown in graphs and for the radon radiation also in tables. In the graphs the abscissae represent the logarithm of the dose and the ordinates the logarithm of the ratio of the coagulation time of the unirradiated sample to that of the irradiated. The similarity of the curves in these graphs to the characteristic curves of photographic emulsions suggested that the primary reaction is a photochemical action on the colloid particles.—*Audrey G. Morgan.*

GRAY, L. H., MOTTRAM, J. C., and READ, JOHN. Some experiments upon the biological effects of fast neutrons. *Brit. J. Radiol.*, Nov., 1940, *13*, 371–388.

Experiments were made dealing with the comparative action of fast neutrons (2.8 MEV)

and gamma rays on mitosis in cultures of chick embryo fibroblasts and on the root of the broad bean. The technique of measuring the dosage is described. By this method it is possible to compare the effects of equal amounts of gamma-ray and neutron energy absorbed by a unit volume of tissue. Curves are given showing the effect of gamma rays and neutrons on these two forms of tissue, and a table which shows a complete summary of the results of quantitative investigation of the biological effects of fast neutrons, and against each effect is shown the relative efficiency of roentgen-ray and gamma-ray ionization determined by direct comparison between the doses of the two kinds of radiation which produce the same biological effects. In all except two cases neutron ionization was more effective in producing biological change than gamma radiation. The difference in shape and size of the mitosis dose curves for gamma rays and neutrons is evidently due to the fact that with gamma rays the ionization is produced by several hundred secondary electrons and with neutrons by a single or at most a few recoil protons.

Other quantitative studies of the biological effects of fast neutrons are reviewed and a hypothesis is advanced to account for the greater relative efficiency of neutrons which seems to be based on plausible assumptions for which the authors hope to obtain histological evidence.—*Audrey G. Morgan.*

Eidinow, Albert. The action of the radiations emitted by (1) radium plaques, (2) unfiltered and filtered radon seeds and (3) intravenous injection of radon dissolved in blood. *Brit. J. Radiol.*, Nov., 1940, *13*, 357–370.

Experiments are described which were made to test the effects of radium and radon on human leukocytes in vitro and on the skin of rats in vivo. A flat square plaque of radium 2 by 2 cm. in size covered with 0.12 mm. silver was applied to the skin of rats. When the plaques were kept in position for twenty-four hours the animals died after three to four days. The time of application was reduced until the minimum lethal dose of surface radiation was determined.

Tables and charts are given showing the lethal doses of radium plaques, filtered and unfiltered radon seeds, and radon dissolved in citrated blood. The technique of preparing this blood is described. It was found that the energy of five hours' application of the plaques described above to rats weighing 50 to 80 gm. is equivalent to that of 2.5 mc. seeds of radon filtered by 0.7 mm. silver or 0.3 mm. platinum given subcutaneously to rats of the same weight or to the intravenous injection of 2.0 mc. radon dissolved in 0.5 cc. citrated rats' blood. This biological method of estimation of dosage agrees with the estimations made by physical methods. The experiments suggest a biological method of standardizing roentgen rays, radium or radioactive sources. Young rats weighing about 50 gm. should be used. The radiations are absorbed directly by the blood and the injury is caused by damage to endothelial cells and to general toxemia.

Leukopenia and the other pathological changes following the application of lethal doses of surface radium radiation were the same as those produced by equivalent doses of radon seeds or radon dissolved in citrated blood.

The rays absorbed can be demonstrated in the blood and organs of the body by exposing them to a sensitive photographic plate. Sublethal doses of radon dissolved in citrated blood and injected intravenously into rats arrest and delay the growth of experimental tumors. Radon dissolved in blood can be used in treatment and causes the same biological changes in the body as the use of roentgen rays or teleradium.—*Audrey G. Morgan.*

Oddie, T. H. A note on dosage data for radium therapy. *Brit. J. Radiol.*, Nov., 1940, *13*, 389–392.

The gamma-ray dosage system developed by Paterson, Parker and Spiers is widely used. Roberts extended it to the use of small rectangular surface applicators and reference is made for details to his article in *Brit. J. Radiol.*, 1938, *11*, 755. This article still further extends it to the dosage of triangular plane areas with surface applicators and to the determination of dosage in cones, prisms, pyramids or tetrahedra of tissue treated with implanted needles. Tables are given showing the percentage corrections necessary for such extended applications of the method.—*Audrey G. Morgan.*

Russ, S., and Scott, G. M. The effect of x-rays upon tumour growth when the tumour itself is not irradiated. *Brit. J. Radiol.*, Aug., 1940, *13*, 267–272.

Some years ago the authors performed experiments which showed that grafts of Jensen's rat

sarcoma grew more readily in the normal tissue of a rat than in adjoining tissue which had been irradiated with roentgen rays or radium. In this article they describe experiments made to determine to what extent it might be possible to check an actively growing Jensen's rat sarcoma by irradiating the tissue around it while the tumor itself was not irradiated at all. The method of lead screening to protect the tumor from the rays is described and illustrated.

It was found that when a dose of approximately 1,200 r was given to the tissue around such a tumor the rate of growth was considerably slowed and in 37 per cent of the cases irradiated in this way (30 out of 82 tumors) the tumor disappeared entirely. This method of irradiation caused practically no injury to the skin—only slight temporary epilation in some cases. Among the 190 control cases which were not treated only 13 disappeared, or just under 7 per cent. In cases in which the tumor was irradiated directly 75 per cent of the tumors disappeared.

Graphs are given showing the logarithmic rate of growth of tumors directly irradiated and that of tumors in which only the bed was irradiated, separate graphs being given for cases in which a small surrounding area was irradiated and ones in which a large surrounding area was irradiated.—*Audrey G. Morgan.*

BARCLAY, A. E., FRANKLIN, K. J., and PRICHARD, M. M. L. X-ray cinematography in research. *Brit. J. Radiol.*, July, 1940, *13*, 227–234.

The apparatus and techniques used in roentgen cinematography in research at the Nuffield Institute for Medical Research, Oxford, are described and illustrated in this article. In their study of the circulation in animals the authors have used both the direct and indirect methods of roentgen cinematography. The two methods complement each other. By means of the indirect method it is possible to record and project the actual speed of movement or even show it in slow motion, while films obtained by the direct method, which are necessarily taken at a much slower rate, provide the finely detailed, life-size pictures that are necessary for accurate study and analysis.—*Audrey G. Morgan.*

GILARDONI, ARTURO. La schermatura catodica dei tubi Coolidge e la sua influenza sulla caratteristica di emissione e sull'illuminazione Röntgen. (The cathode screening of the Coolidge tube and its influence on the characteristics of roentgen emission and illumination.) *Radiol. med.*, April., 1941, *28*, 218–223.

The author gives a description of the Coolidge tube and curves showing the effect of the cathode screening on the emission and characteristics of the roentgen rays emitted.

He concludes that tubes with a large screen effect have the advantage over those with a small screen effect of furnishing a roentgen illumination stronger by about 40 per cent, for an equal number of kilovolts of tension and a medium number of milliamperes. They also have a greater capacity for autostabilization of the radiation emitted when there are variations in the tension of the current. Tubes with a large screen effect can be used to advantage in diagnostic apparatus of low potential, up to about 25 milliamperes, and in treatment apparatus with a Villard circuit.—*Audrey G. Morgan.*

BELL, G. E., and SMITH, E. E. The optimum densities of radiographs. *Brit. J. Radiol.*, Aug., 1940, *13*, 285–288.

The visibility of a defect on a roentgenogram depends to a great extent on the photographic density of the background. This article considers theoretically and experimentally some of the photographic factors for the purpose of determining the optimum range of densities.

It is found that the actual difference in blackening ΔB between the roentgenogram of the defect and the uniform background depends on the density of the roentgenogram and, at least up to densities of 5, increases with increasing density. Generally however a roentgenogram is examined by the eye and the blackening difference ΔB which can be detected is a function of the brightness of the surface examined and depends on the value of the Fechner fraction appropriate to the circumstances. The brighter the surface the smaller the value of ΔB which can be appreciated, at least in the range examined. The combined effect of photographic sensitiveness and the sensitiveness of the observer's eye gives a range of densities for which the resolution of a roentgenogram is greatest. If the roentgenogram is of good quality this range of optimum densities extends from about 1 to 2.—*Audrey G. Morgan.*

Richard T. Dooner

RALPH S. BROMER

President of the American Roentgen Ray Society

1942–1943